

California MEDICINE

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Antibiotics and Chemotherapy

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IN THE HISTORY of man's struggle against infectious diseases and epidemics, certain great discoveries stand out. By far the most important of these was the recognition of the fact that bacteria, protozoa, viruses, and other microscopic forms of life are the agents responsible for causing infectious diseases.

The ancients designated as pests, plagues, or pestilences those diseases which were epidemic in nature. They frequently ascribed such epidemics to the wrath of the gods. A study of the Bible convinces one of the early remarkable understanding of the infectious nature of diseases, methods of prevention, and even of treatment. Deuteronomy alone abounds in such illustrations. In Chapter XXIII, this passage: "And a place shalt thou have without the camp, whither thou shalt go forth abroad: And a spade shalt thou have with thy weapons; and it shall be, when thou sittest abroad, that thou shalt dig therewith, and shalt afterward cover that which cometh from thee." In Chapter XXIV: "Take heed of the plague of leprosy, to observe diligently, and to do according to all that the priests, the Levites, may instruct you; as I have commanded them, so shall ye observe to do." And in Chapter XXVIII: "The Lord will cause the pestilence to cleave unto thee, until it have consumed thee from off the land, whither thou goest to possess it. The Lord will smite thee with consumption, and with fever, and with inflammation, and with extreme burning."

From the Institute of Microbiology, Rutgers University.
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Gradually it became recognized that such diseases are caused by living organisms, which are transmitted directly or indirectly from the diseased to the healthy. The final recognition of the microbial origin of disease came during the latter part of last century.

Louis Pasteur stands out as the central figure in establishing the fact that bacteria and different other microbes are largely responsible for the causation of infectious diseases. Although he himself did not isolate many of the infectious agents, he established the significance of infection, immunization, and vaccine therapy, the three broad principles that dominated the recognition of nature and treatment of infectious diseases before the recent advent of chemotherapy. He contributed, incidentally, in large measure, to the domestication of microbial forms of life. Pasteur's work led to a tremendous upsurge of efforts to correlate the occurrence and distribution of bacteria and other microorganisms with the causation of specific diseases. Experimental procedures were devised for studying the nature of the disease-producing agents and for the preparation of various biological and chemical agents for the control of infectious diseases.

Robert Koch is the other great pioneer in the field of discovery of causation of disease and methods of treatment. His study of the life cycles of bacteria and his methods for the isolation, cultivation, and staining of bacterial agents served further to advance the science of microbiology and led him to the discovery, in 1882, of the tubercle bacillus, and thus to establishment of the infectious nature of tuberculosis. Although his other great discovery, tuberculin,

which he thought would serve as the therapeutic agent for combating this infectious disease did not justify his expectation and proved to be the first failure among the many "cures" for the treatment of tuberculosis which were to follow, he established, nevertheless, an important principle of infection which came to be known as the "Koch effect."

Following these two groups of discoveries, a host of investigators, including bacteriologists, protozoologists, mycologists, and virologists, isolated organisms that cause numerous infectious diseases that afflict man and his domesticated plants and animals, established the mode of transmissions of such diseases, and discovered means of prophylaxis and therapy.

It was the search for chemical substances or drugs which could be used in the treatment of infectious diseases that led to another great discovery in the field. Paul Ehrlich, noted for his contribution to immunology, is credited with being the "father of chemotherapy." He not only established the great potentialities of certain dyes and arsenical agents in combating a variety of diseases, such as syphilis, but he pointed to the great potentialities of synthetic chemistry in opening a way for the final control of human diseases. The work of Ehrlich was opposed by a few, but it was readily accepted by chemists and microbiologists, and served to arouse the medical world to the belief that before very long new drugs would be found that would act in a similar manner upon bacterial and other diseases.

Although bitter disappointment soon followed, Ehrlich's prophecy was fulfilled a quarter of a century later with the discovery of the sulfa drugs. The introduction of these compounds ushered in a new era in chemotherapy. It was now established beyond question that not only protozoan and spirochetal diseases, which were successfully treated with arsenical compounds, but bacterial infections as well could be effectively combated by generalized treatment with chemical drugs. Thus the basis was laid for bacterial chemotherapy.

In rapid succession, one drug followed another. Each proved to have certain advantages over the previous ones. New types of compounds were soon added, like the sulfones, which were believed to be able to do for tuberculosis what the others did for most of the bacterial infections.

But there appeared to be a certain limit beyond which these compounds could not reach. There still remained a great many diseases which did not respond to the sulfa drugs, including many caused by Gram-positive and Gram-negative bacteria; the various forms of tuberculosis did not respond well to the sulfones; the virus diseases were not affected at all. Furthermore, these compounds were found to

produce frequent toxic reactions and gave rise, under certain conditions, to drug-resistant strains of bacteria.

Fortunately, even before the limitations of the synthetic compounds were fully recognized, a dramatic advance was made in chemotherapy through the microbiological research that led to the discovery of antibiotics. Several major groups of microorganisms, comprising certain bacteria, molds or fungi, and actinomycetes, were found capable of producing various metabolic products which had the capacity of inhibiting the growth of and even of destroying disease-producing bacteria, not only in the test tube but also in the human and animal body. This fundamental principle was first recognized in 1939-1940. It brought about at once a change in the whole problem of chemotherapy. Medical science was revolutionized. Diseases never before believed to be susceptible to therapy were treated with remarkable effectiveness. Old drugs were replaced by new ones, which were more effective and less toxic. Even such apparently resistant diseases as brucellosis and tuberculosis became subject to therapy. One of the most important chapters in the history of science and medicine was written before our eyes.

The discovery of antibiotics served to encourage, rather than discourage, chemical synthesis. New compounds are being tested daily. I need hardly dwell upon some of the substances developed during the war for the treatment of malaria and various animal parasites. The discovery of the effectiveness of isonicotinic acid in the treatment of tuberculosis serves as further evidence of the great potentialities in this field and of the great future for chemotherapy.

The continued search for new antibiotics and the chemical synthesis of new compounds are now proceeding hand in hand, toward the ever-expanding battle against infectious diseases and toward the final triumph of the human mind.

Since the early days of microbiology, the phenomenon known as antagonism or antibiosis has been observed by the student of mixed populations, in soil or in water basins, in mixed infections, and even by the casual observer of contaminated plate cultures of microorganisms. Although the ability of various bacteria and fungi to produce antimicrobial substance has thus long been appreciated, recognition of the great chemotherapeutic potentialities of these substances, now designated as "antibiotics," is of very recent origin. Hardly a dozen years ago, these substances were spoken of as lysins, toxins, bacteriolysins, bacteriotoxins, bacteriostatic, bactericidal and bacteriolytic substances, antibacterial or antagonistic agents, lethal and staling principles, and by a variety of other designations.

It is sufficient to cite in this connection the concepts of Dubos in 1939, who has made a highly im-

portant contribution to the development of this subject. Having succeeded in isolating from the soil an organism which could decompose soluble polysaccharides extracted from certain bacterial pathogens, he proceeded to develop methods for the isolation of microorganisms capable of attacking not only specific cell components, but also the intact living cell itself. This work resulted in the isolation, in 1939, of a bacterial culture which produced a soluble agent that had the capacity to attack and cause lysis of living cells of susceptible Gram-positive bacteria. He spoke of it as "a bactericidal agent extracted from a soil bacillus."

These concepts illustrate the prevailing attitude toward the phenomenon of antagonisms and the production of antibiotics. With certain few exceptions, the chemotherapeutic significance of these compounds was hardly appreciated. Practical applications were thought to be limited. They were looked upon largely as microbiological curiosities.

The mechanisms responsible for the antagonistic properties of microorganisms were not sufficiently understood. Numerous theories were proposed to explain the reactions involved. They included competition for nutrients, competition for space, exhaustion of certain elements in media, physicochemical effects, and production of specific growth-inhibiting substances. There was a special appeal in the concept of "struggle for existence," which was hardly justified on closer examination.

This confusion contributed to a lack of recognition of the potential value of the antibiotic substance in human and animal therapy. When Alexander Fleming described penicillin in 1929, he thought in terms of obtaining cultures of Gram-negative bacteria free from Gram-positive forms. Although he fully appreciated the great therapeutic potentialities of this type of substance, no further investigation of this problem followed for nearly a decade. It was for this reason that neither Raistrick, who attempted to isolate penicillin in 1932, nor Reid, who tried to repeat Fleming's experiments in 1935 in this country, was successful in unravelling this problem.

This was true also of the various investigations of the antibacterial substances produced by different bacteria. It is sufficient to list the numerous studies on pyocyanase, produced by *Pseudomonas aeruginosa*, and the products of *Bacillus subtilis*, *B. mycoides*, and other spore-forming bacteria. Even less can be said of the substances produced by actinomycetes, of which only two enzyme-like preparations were recognized before 1940, in spite of the fact that many of these organisms were known to exert a pronounced growth-inhibiting effect upon various bacteria and fungi. As late as 1938, none of the substances of microbial origin, with the possible exception

of pyocyanase, received any consideration as agents with therapeutic potentialities heralding a new era in medicine.

Our modern knowledge of the production and utilization of antibiotics dates back only to the last 13 or 14 years. The isolation of the tyrothricin complex from a spore-forming soil bacterium in 1939, soon followed by the re-isolation of penicillin from fungi in 1941, and by the isolation of actinomycin in 1940 and of streptothricin in 1942 from cultures of actinomycetes, pointed to the great potentialities of microorganisms as producers of antibiotics.

These contributions opened a new chapter in microbiology and especially in human and animal therapy. In this brief span of time, large numbers of well-defined chemical substances now designated as antibiotics have been isolated and tested for their antimicrobial properties. The actinomycetes alone have yielded nearly 100 compounds or preparations. Hundreds of thousands of cultures were isolated from soils, water basins, composts, and other natural substrates. They were examined for their ability to inhibit the growth of pathogenic and saprophytic bacteria, fungi, viruses, protozoa, and insects. Many have been studied further for their capacity to produce antibiotics. Numerous books have been written on the subject. Special journals in various countries and in different languages are devoted to it. Penicillin, streptomycin, bacitracin, chloramphenicol, polymyxin, aureomycin, terramycin, neomycin, and erythromycin have taken an important place in the treatment of numerous infectious diseases caused largely by bacteria, spirochetes, rickettsiae, and some of the larger viruses. Several other compounds are known to be promising therapeutic agents.

Antibiotics are produced by microorganisms and are not to be confused with plant products, such as quinine, and with certain animal products, such as lysozyme, that may possess similar properties. Neither are they to be confused with various organic acids and alcohols that are produced by microorganisms and that are active only in high concentrations.

The formation of antibiotics is limited to certain species and frequently to certain strains of organisms. On the one hand, penicillin is produced by a number of strains of a great variety of fungi belonging largely to the genera *Penicillium* and *Aspergillus*. Streptomycin is produced only by certain strains of *Streptomyces griseus* and of certain other species of *Streptomyces*. Some of these are able to form chemical modifications of this antibiotic, as in the case of hydroxystreptomycin produced by *S. griseo-carneus*, or they may give rise to quantitatively different mixtures of the antibiotics, as streptomycin vs. mannosido-streptomycin. Other strains of *S. gri-*

seus may form other antibiotics, such as streptocin and candicidin.

By proper strain selection and by changing the composition of the medium it is possible to increase greatly the yield of the antibiotic and frequently to induce certain chemical variations in its molecular structure as in the case of the different penicillins.

In searching for new antibiotics, it is advisable to consider certain fundamental principles which they should possess before they can qualify as suitable chemotherapeutic agents:

1. They should be selective in their action against bacteria and other microorganisms, and not act as general antiseptics or disinfectants.

2. They should be effective against those microorganisms that are not now subject to the action of antibiotics, or they should be more effective or less toxic than the agents already known.

3. They should exert their antimicrobial activity in the presence of body fluids, and should not be inhibited by substances present in the blood or be destroyed by tissue enzymes.

4. They should be well tolerated when injected into animals in amounts required for combating infections.

5. In concentrations necessary to affect the infectious agent, they should not damage the leukocytes in the blood or be injurious to body tissues.

6. They should be excreted readily, but not too rapidly, from the animal body, and should not accumulate to produce undesirable after-effects.

7. They should not favor the rapid development of resistance among sensitive organisms.

The potential synergistic properties of a new antibiotic with another antibiotic or with a synthetic compound must not be overlooked, even though the new agent may not in itself play an important role in chemotherapy.

The various antibiotics so far isolated and recognized can be classified on the basis of their chemical composition, their antimicrobial spectra, their toxicity to animals, or their chemotherapeutic potentialities.

Chemically, antibiotics range from fairly simple to highly complex compounds. Some contain only carbon, hydrogen, and oxygen. Others are more complex and contain nitrogen (streptomycin— $C_{21}H_{37}O_{12}N_7$), or nitrogen and sulfur (penicillin— $C_9H_{11}O_4SN_2R$), or nitrogen and chlorine (chloramphenicol— $C_{11}H_{12}O_5N_2Cl_2$). Some are polypeptides (gramicidin, subtilin, and bacitracin), proteins (colicins), or benzene ring compounds. Only very few antibiotics have so far been synthesized, notably penicillin, clavacin, and chloramphenicol; of these, only chloramphenicol has found practical applica-

tion in therapy. Some of the antibiotics represent single chemical entities, whereas others are made up of several closely related compounds. The latter is true for the penicillins, the streptothricins, the streptomycins, and the aureomycin-terramycin complex. The individual antibiotic entities may vary in their antimicrobial spectra, in toxicity to animals, in stability, and in activity *in vivo*.

Antibiotics also vary greatly in their antimicrobial spectra. Some are active upon a great variety of bacteria, and even upon fungi, rickettsiae, and other groups of microorganisms. Others have very narrow spectra, and are active only upon certain groups of organisms, such as mycobacteria, yeast-like fungi, or certain viruses. Clavacin has a very wide spectrum; penicillin and streptomycin have narrower spectra. Chloramphenicol, aureomycin, terramycin, and erythromycin are active against various bacteria as well as against rickettsiae and some of the larger viruses. Viomycin, esperin, and nocardin are active only upon the mycobacteria; the polymyxins are active largely upon Gram-negative bacteria. Actidione, fradicin, fungicidin, antimycin, ascosin and candicidin are active only upon fungi, with considerable variation in their spectra.

Antibiotics also vary greatly in their toxicity to animals: penicillin is least toxic; actinomycin, streptomycin, and xanthimycin are among the most toxic. Clinically, antibiotics vary from important chemotherapeutic agents that are used in the treatment of a great variety of infections, to certain compounds, like tyrothricin, bacitracin, and polymyxin, which have only limited applications.

The microorganisms which are capable of forming antibiotics frequently represent large and variable groups. This is true of the numerous members of the *Penicillium notatum*-*P. chrysogenum* group, which yield various penicillins; the *Streptomyces griseus* group, which produce the streptomycins; the *S. lavendulae* group, which form streptothricin and a variety of other substances; the *S. aureofaciens*-*S. rimosus* group, which produce aureomycin and terramycin; and the *B. subtilis* group, which is responsible for more than a dozen compounds possessing antimicrobial properties. There are certain pronounced differences between the various members of these groups of microorganisms. The numerous strains of *Penicillium* vary not only in their quantitative production of penicillin, but also in the nature of the particular type of penicillin.

The fungi have so far yielded one antibiotic that has found practical application, that is, penicillin. The bacteria, notably the spore-forming organisms, have contributed several important agents, mostly polypeptides, some of which, such as tyrothricin, bacitracin, and polymyxin, have found certain applications in therapy. The non-spore-forming bacte-

ria have contributed several antibiotics, of which pyocyanase formerly received much consideration. More recently nisin, a product by a micrococcus, showed at first much promise for the treatment of tuberculosis; this has not been confirmed. The colicins have also received much consideration. The most important antibiotics discovered since penicillin have been obtained largely from cultures of actinomycetes, all from members of the genus *Streptomyces*. These include not only the antibacterial and antifungal agents already listed, but also various antiviral and possibly antitumor agents, which one can only hope may prove to be effective.

Some antibiotics are acids, others are bases, still others are amphoteric compounds. Some are readily soluble in water, others are soluble in organic solvents. Some are heat-stable and others are heat-labile. Some have their optima at a basic reaction, others at a neutral or acid reaction. Some are readily absorbed from the digestive system into the body fluids, others are not. Antibiotics vary, therefore, in their practical utilization for disease control. Some are most effective orally, others parenterally, still others topically. Among the many antibiotics that have so far been isolated, only very few have found practical application. These are, in order of their discovery:

Tyrothricin has a narrow antibiotic spectrum and is active primarily against Gram-positive bacteria and cocci. It tends to exert a hemolytic effect upon the blood, which limits its use to topical applications.

Penicillin is still probably the most important antibiotic or group of antibiotics discovered so far. It has a fairly broad spectrum, although it is active chiefly against Gram-positive bacteria, various cocci, and spirochetes. It is the least toxic of all. It possesses certain limitations, chief among which are lack of activity against many bacteria, a certain degree of sensitization of many individuals, and the gradual development of resistance to it among certain sensitive bacteria.

Streptomycin tends to fill the gap left by penicillin. Although not so potent, on a weight basis, it is highly effective against a variety of diseases not known previously to be subject to any form of therapy. It has found extensive application in the treatment of tuberculosis, as well as of numerous infections caused by Gram-negative bacteria, such as tularemia and brucellosis, and various Gram-positive bacteria, especially those that have become resistant to penicillin. The limitations of streptomycin comprise the potential causation of vestibular disturbances and its effect on the auditory system when used in large doses, and the rapid development of resistance among sensitive bacteria after prolonged contact with it. Streptomycin and penicillin form an

ideal combination for the treatment of numerous diseases.

Chloramphenicol, *aureomycin*, and *terramycin* are active upon various Gram-positive and Gram-negative bacteria, as well as upon rickettsiae and some of the larger viruses. They are usually administered orally and have found extensive application in the treatment of such diseases as typhoid fever, typhus fever, whooping cough, and trachoma.

Among the other antibiotics that have become established as chemotherapeutic agents, it is sufficient to mention *bacitracin*, *neomycin*, and *polymyxin*. These compounds tend to exert a somewhat toxic effect when administered parenterally. The first and last also possess narrow spectra. They are, therefore, used largely topically and orally; they are useful in cases of generalized infections that are not readily controllable by other forms of therapy. Neomycin is used alone or in combination with other agents for the treatment of various infections, both orally and topically.

UTILIZATION OF ANTIBIOTICS

Antibiotics have so far found several important fields of application, which can be briefly summarized as follows:

1. Control of numerous infectious diseases of man.
2. Control of diseases of domestic animals.
3. In the nutrition of non-ruminant animals.
4. In the preservation of biological materials, such as bull semen and virus preparations.
5. In certain plant diseases.

There are other potential uses, not as yet clearly understood or developed, as in seed germination and in plant growth.

It is in the treatment of human diseases that antibiotics have made their greatest contribution. It may be truthfully said that antibiotics have revolutionized medical practice. A brief summary may therefore be justified of the role that antibiotics are now playing in the control of various known human and animal diseases.

1. *Diseases caused by cocci (streptococci, pneumococci, staphylococci, gonococci) and various Gram-positive rod-shaped bacteria, comprising aerobic and anaerobic organisms.* These bacteria are highly sensitive to penicillin, to streptomycin, and to a number of other antibiotics, notably aureomycin, terramycin, neomycin, bacitracin, tyrothricin, and erythromycin. These antibiotics have the capacity to attack in a highly efficient manner all of the infections caused by these bacteria. Organisms that become or are resistant to one antibiotic are sensitive to one or more of the others. Recently, there have

come into popular use combinations of two antibiotics, such as penicillin and streptomycin, bacitracin and neomycin, which are usually more effective than a single agent.

2. *Diseases caused by Gram-negative bacteria*. These are, for the most part, resistant to penicillin, to bacitracin, and to some of the other antibiotics. They are sensitive to streptomycin, chloramphenicol, aureomycin, neomycin, and terramycin, which have found extensive application in the treatment of infections caused by these bacteria. In some cases, as in whooping cough and typhoid, one antibiotic, such as chloramphenicol, is preferable to others. In other cases, as in tularemia, another is more effective, such as streptomycin. In still other cases, as in urinary tract infections, several substances are effective, and can thus be used almost interchangeably, notably, aureomycin, terramycin and neomycin. Certain antibiotics are particularly effective in the treatment of certain types of infection, as in the use of polymyxin for *Pseudomonas* infections. Utilization of the synergistic action of two substances, such as aureomycin and streptomycin, or of an antibiotic with a synthetic agent, such as streptomycin and sulfadiazine, in the treatment of certain infections, offers considerable promise of exerting a greater effect, and tends to overcome the danger of potential development of resistance among the sensitive organisms.

3. *Diseases caused by acid-fast bacteria*. Because of their peculiar characteristics, these diseases are among the most resistant to chemotherapy. The discovery that streptomycin can be utilized in the treatment of tuberculosis has provided a great stimulus to the search for new antibiotics and synthetic compounds that possess similar properties. It has aroused hope that the control of this highly important group of diseases may at last be within our reach. The fact that, among the antibiotics, streptomycin is not alone in this respect is indicated by the latent potentialities of a number of other antibiotics, notably, neomycin, viomycin, mycomycin, and nisin. The possible development of strains of *M. tuberculosis* resistant to streptomycin has suggested the supplementary use of other agents, such as para-amino-salicylic acid. The recent introduction of isoniazid for the treatment of this group of diseases has presented new problems and aroused greater hope.

The treatment of leprosy has not yet been solved satisfactorily, although some antibiotics have been found to be effective. Indications are that, sooner or later, this ancient disease of man will become subject to chemotherapy.

4. *Spirochetal diseases*. Several antibiotics, notably penicillin and bacitracin, have a remarkable effect upon syphilis and other diseases caused by spirochetes. The utilization of antibiotics in the

treatment of these infections has gradually superseded the use of salvarsan and other methods of treatment in vogue before the advent of antibiotics.

5. *Rickettsial diseases*. These diseases, comprising typhus fever, scrub typhus, spotted fever, and a variety of others, are readily subject to therapy by a number of antibiotics. These include chloramphenicol, aureomycin, terramycin, and erythromycin, all of which appear to be able to control virtually this whole group of infections. The choice of the particular drug depends largely upon circumstances.

6. *Fungous diseases*. Various antibiotics are known to possess pronounced fungistatic and fungicidal properties. Unfortunately, most of them are too toxic for general use. This is true of actidione, fradicin, fungicidin, and others. Although none has as yet found application in the generalized treatment of fungous infections, there are indications that some antibiotics, such as fungicidin RAW, rimicidin, ascosin, and candididin, will soon be found capable of controlling some of these diseases.

7. *Protozoan and other diseases due to animal forms*. No true antibiotic is now known to be significantly effective against diseases caused by the malarial and certain other important protozoan organisms. The ability, however, of various agents to affect amebae, trypanosomes, trichomonads, and other protozoa has been definitely established. Some of these substances have already found practical application in chemotherapy. This is true, for example, of aureomycin, terramycin and fumigallin, which are used successfully against amebic dysentery, although it is claimed that the favorable effect consists largely in killing the bacteria upon which the amebae feed.

8. *Viral diseases*. Some of the larger viruses, notably the psittacosis and lymphogranuloma venereum groups, are susceptible to various antibiotics, such as chloramphenicol, aureomycin, and terramycin. The usefulness of these in such viral infections as trachoma has also been definitely established. Their use in other viral diseases, such as mumps, infectious mononucleosis, influenza, and so-called viral pneumonia, requires further confirmation or elucidation. No antibiotic has so far found practical application in the treatment of diseases caused by the smaller viruses, of which the causative agents of the common cold and of poliomyelitis are most important. Recently reports of the formation of specific antiviral agents against some of the viruses were published. The practical potentialities of these preparations, however, have not been established.

9. *Neoplasms*. Tumor or cancer cells are known to be subject to the action of various microorganisms and their products. It is sufficient to mention the effect of certain bacteria such as *Sporosarcina*

ureae, of trypanosomes such as *Trypanosoma cruzi*, and of fungi belonging to the *Aspergillus fumigatus* order. The effective agents so far isolated have proved to be too toxic for practical use. The evidence obtained suggests, however, that sooner or later, suitable chemotherapeutic agents will be found.

10. *Shock and radiation diseases.* When the human or animal body is subject to shock or to the effect of injurious radiations, it becomes a victim of the otherwise uninjurious intestinal flora and other bacteria inhabiting the human body. In combating the injurious action of such bacteria, certain antibiotics, such as neomycin and aureomycin, may prove to be highly helpful. These phenomena may be of tremendous importance in certain emergencies upon which we need not dwell here.

The story of tuberculosis is that of a continuous battle of mankind against one of its greatest enemies, one that has a particular capacity for attacking its victims at a time of great stress, as in war and in immediate postwar periods. No wonder that this dreadful disease has been called the "Great White Plague"! Less than a decade ago, even after the introduction of the sulfa compounds and penicillin, the medical profession was inclined to the belief that no drug effective against tuberculosis would ever be found. The discovery of streptomycin pointed a way to successful chemotherapy of the disease. It has aroused hope that before very long this scourge of mankind will be brought under complete control. Numerous antibiotics are now known to possess anti-tuberculosis properties. Streptomycin, alone or combined with para-aminosalicylic acid or with isoniazid, is a highly important agent in the treatment of tuberculosis.

Numerous clinical investigators followed the early studies of Hinshaw and Feldman in emphasizing the fact that streptomycin reversed the trend of tuberculosis and that the majority of the patients treated were improved. This antibiotic was found to bring about a rapid fall in temperature and accompanying symptomatic improvement and a regression of pulmonary lesions. It has found a definite place in the treatment of miliary tuberculosis and tuberculous meningitis, tuberculous sinuses and fistulas, of bone and joint tuberculosis, and of various forms of early and pulmonary tuberculosis.

The conclusion was reached that the most significant contribution of antibiotics and synthetic compounds in the treatment of tuberculosis is that they have demonstrated that the chemotherapy of this disease, like that of most other infectious diseases, is possible. In my recent travels through southern and western Europe, I was profoundly impressed by the successful results obtained in the treatment of certain forms of tuberculosis by streptomycin. Re-

covery rates as high as 50 to 75 per cent in cases of meningeal and miliary tuberculosis were claimed.

As one surveys the broader aspects of the subject of antibiotics; as one realizes that a mere fraction of the microorganisms present in numerous soil types throughout the world, in various water basins, on numerous food products, and on many other substrates have so far been examined for their ability to produce antibiotics; as one visualizes the great variety of chemical compounds which are formed by these organisms and which have the capacity of inhibiting the growth of and even of destroying other microorganisms; as one finds that some of the isolated compounds are not very toxic to animals and possess properties which would render them desirable chemotherapeutic agents—one is inclined to become optimistic and to hope that, before long, all human and animal infections, and possibly plant infections as well, can be combated if not completely eliminated by the utilization of antibiotics.

One may stop, therefore, and analyze the problems in the field of antibiotics that face us at present. We recognize the need for:

1. New antibiotics more active against infectious agents that have become resistant to known antibiotics.
2. New antibiotics capable of exerting a synergistic action, when combined with other known chemical or biological agents, in combating chronic diseases, such as brucellosis, leprosy, and tuberculosis.
3. Antibiotics suitable for combating fungous diseases, filterable viruses, and neoplastic diseases.
4. A better understanding of the mode of action of antibiotics upon various microorganisms, of the mechanism of the development of resistance, and the problem of overcoming it.
5. A better understanding of the role of antibiotics in animal nutrition and the over-all effect upon the human body.
6. Antibiotics to be used in the control of plant diseases.

The search for new antibiotics will continue. New approaches will be found and new screening methods will be developed. Many substances will be discovered which will prove to be better than those now known, or which will act upon diseases not susceptible at present to chemotherapy. Finally, more profound knowledge of the physiological and biochemical mechanisms of the action of antibiotics upon bacteria, viruses, and other pathogenic organisms may help to clarify the still obscure aspects of their mode of action, and thus possibly lead to the discovery, or even to the synthesis, of new and better chemotherapeutic agents.

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Double Contrast Visualization of Joints

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SINCE CONVENTIONAL roentgenographic studies often do not supply the information needed for evaluation of intra-articular derangements, several modifications of ordinary procedures have been developed to obtain better visualization. All have objectionable features, either of inadequacy or of harm to the patient.

(a) Forceful traction to permit contrast visualization of cartilages in the knee and other joints has met with a degree of success. Particularly in the case of smaller joints, a vacuum spacing may be produced by this means. Within a period of a few minutes, however, diapedesis of fluid occurs within the joint to an extent that the intra-articular cartilages and other intra-articular components no longer can be visualized. And of course in cases in which there is already fluid in the joint owing to effusion, this method is impractical. Even if the knee is relatively normal, the medial meniscus can be visualized by this means in only about 70 per cent of cases; the lateral meniscus, in less than 7 per cent. The main attribute of this means of solving the problem is the relative simplicity of the procedure. There are many exponents for it—Nordheim,¹⁹ Evans,⁹ Long,¹⁶ Gershon-Cohen,¹⁰ and others.

(b) Injection of "positive media" such as solutions of inorganic iodides and organic iodine compounds including iodized oils. Particular reference is suggested to the works of Burman, Tunick and Pomeranz,⁶ Boyd,⁴ Keller,¹⁴ Jepson¹¹ and Jowett.¹² Most observers have expressed condemnation of this procedure. The synovial lining of joints is far more sensitive than epithelial-lined channels or sinuses through granulomatous or fibrous tissue recesses. Severe pain is produced by injection of almost any of the media. Intra-articular fibrosis has sometimes ensued.

(c) Injection of gas provides so-called "negative" contrast. Various gases have been used including air, nitrogen, nitrous oxide, ethylene, carbon dioxide and oxygen. Air remains in the joint too long. Carbon dioxide is too rapidly absorbed. Nitrous oxide and ethylene have been recommended but the authors' experience is limited to the use of oxygen. Pulmonary embolus has been reported even with the use of oxygen, although this can be avoided by injecting only a limited quantity (50 cc. to 100 cc.) pre-

ceded by aspiration to make sure that the needle is not in a vein. There should never be a direct connection between the gas tank and the joint. This technique has many advocates. Reference is suggested particularly to the writings of Kleinberg,¹⁵ Simon, Hamilton and Farrington,²² Quaintance,²⁰ Mohlmann and Madlener,¹⁸ Anderson,¹ Brook, MacKenzie and Smith,⁵ Meschen and McGaw,¹⁷ Kelikian and Lewis,¹³ Sachs, McGaw and Rizzo,²¹ and Cullen and Chance.⁸

(d) The combination of ray-opaque medium and ray-transparent medium has been used for "double contrast roentgenography." The procedure has been criticized as too complicated, and apparently less developmental work has been done on it than on any of the other methods mentioned. It does have sponsors, however, including Bircher and Oberholzer,² Clausen,⁷ and Blonek and Wolf.³

(e) Endoscopy has been attempted but there are many criticisms of this procedure, both on account of the risk involved and the diagnostic inefficiency.

"DOUBLE CONTRAST" STUDIES

The authors carried out studies with the "double contrast method." In this procedure, sodium iodomethamate (Neo-Iopax[®]) is introduced with sterile precautions, after which the joint is moved by alternating flexion and extension and by ballottement of the patella (in the case of the knee) to spread the material. As a rule 10 cc. of dye is injected, and then most of it is removed by aspiration. This may be repeated.

As the medium is irritating it is necessary to anesthetize the synovial membrane. For this purpose 2 per cent metycaine is used and the solution is in-

jected intracutaneously, subcutaneously and, several cubic centimeters of it, within the joint. Ten minutes later the dye is injected. Besides preventing pain from the dye, anesthetization produces relaxation, which facilitates the manipulation for the different positionings required in the roentgenographic procedure itself.

After the iodide material has been introduced and distributed into all recesses of the joint and the surplus is withdrawn, oxygen is injected from a 100 cc. sterile syringe. As the rubber tubes used for connection to the oxygen tank must also be aseptic, precautions must be observed in making the connection. The "open" end of the rubber tubing should contain a sterile cotton plug (filter). Oxygen should be introduced into the tubing and a sterile needle used to withdraw the desired amount from it (in the case of the knee as much as 100 cc.). The oxygen then is injected into the joint.

After the examination is completed, the synovial cavity is washed with sterile saline solution to eliminate all the iodide. For this purpose the authors use 12 successive fillings and emptyings through the needle although perhaps so much washing is not necessary except in cases of iodine sensitivity.

ROENTGENOGRAPHIC TECHNIQUE

As there is often a little solution still in the knee joint at the time of oxygen injection, the pictures should be taken with the patient prone and the foot of the table elevated 20 to 30 degrees so that the fluid may gravitate into the suprapatellar pouch and be out of the way of the structures being examined. For visualization of the menisci and other intra-articular structures, it is well to flex the knee about 15 degrees and to apply traction to the leg to separate the cartilages. Adduction or abduction can be used to open the space at the outer or inner side. For visualization of the posterior articular cartilages of the patella, the knee should be extended and the patient should relax the quadriceps muscle. An elastic bandage applied over the suprapatellar pouch may help keep the oxygen in the main portion of the joint. To show the posterior pouch in the lateral view, the knee should be flexed 60 to 70 degrees.

For such studies it is advisable to use higher than conventional kilovoltage—70-80 k.v. even for a knee of average dimension. Stereoscopic views are worth while and special views may be indicated by the nature of clinical observations.

INTERPRETATION

Interpretation of the double contrast arthrograms is slow to be learned.

Figure A illustrates some of the tissues of a normal knee joint visualized by this method. The needle

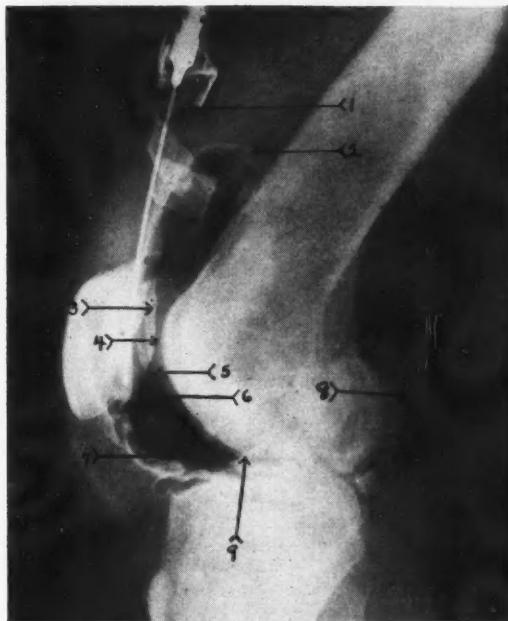


Figure A.—Double contrast arthrogram of normal knee. (1) Cannula remaining in during examination. (2) Upper limits of distended suprapatellar pouch. (3) Border of bony part of patella near its articular cartilage. (4) Border of articular cartilage of patella. (5) Border of the bony portion femoral condyle covered with articular cartilage. (6) Articular cartilage femoral condyle. (7) Intra-articular ligament (ligamentum mucosum). (8) Posterior synovial lining. (9) Anterior cruciate ligament.

was left in for this study but ordinarily it is removed for roentgenography and reinserted for the aspiration and flushing. Note that the film of opaque medium adhering to the surfaces is of minimal degree, yet it actually renders the surfaces far more visible than when oxygen alone is used.

Figure B illustrates findings in chondromalacia of the patella. Compare the shadow of the articular cartilage of the patella, which is roughened at its articular border and has irregularity of opacity in its outline, with the surface outlines of the normal cartilage of the patella in Figure A.

Cartilaginous pathologic changes may be visualized as ragged or irregular outlines of the opaque medium due to the penetrating crevices, partially detached fragments or roughened surfaces. Thinning of the cartilage or absence of it can be recognized by the narrowness of spacing between the surface layer of the opaque medium and the outlines of the articular osseous cortex.

Figure C illustrates the superior demonstration of the semilunar cartilages by this method. In case of a detached cartilage, an opaque marking is to be expected on the capsule in the region whence the cartilage was detached, with transparency owing to



Figure B.—Double contrast arthrogram of chondromalacia of patella. (1) Roughening of border of articular cartilage of patella.

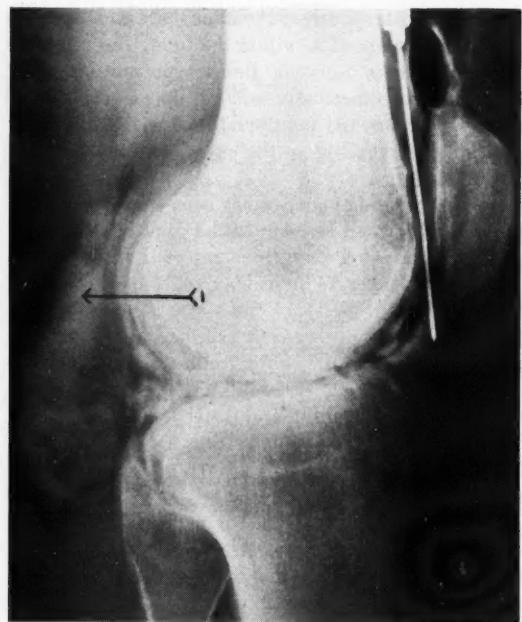


Figure D.—Double contrast arthrogram of joint hernia. (1) Hernia sac distended with synovial fluid containing low concentration of dye and gas bubbles.

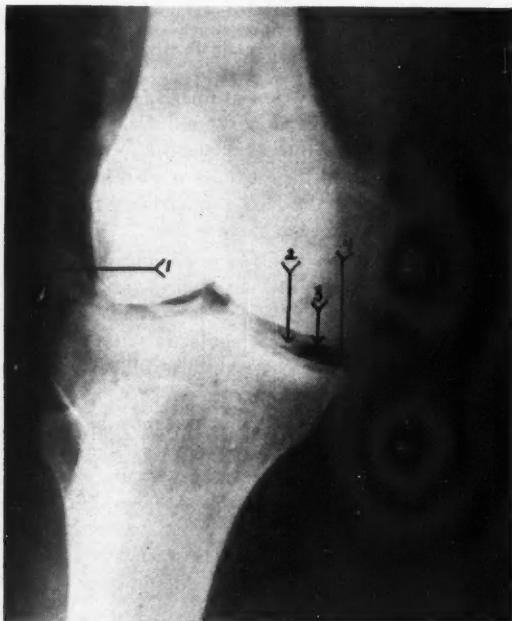


Figure C.—Double contrast arthrogram of bucket handle fracture of medial meniscus. (1) Lateral meniscus normal. (2) Medial meniscus displaced. (3) Articular cartilage of femoral condyle. (4) Position that should be taken by medial meniscus is vacant. Note opaque medium adhering to the capsule where cartilage is detached.

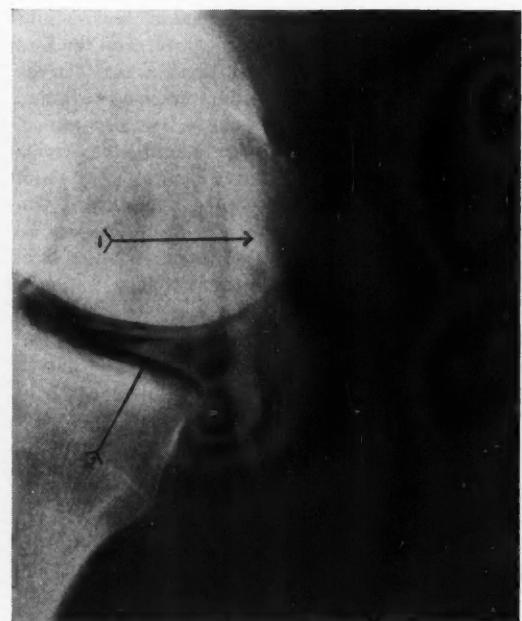


Figure E.—Double contrast arthrogram oblique view of joint hernia. (1) Synovial hernia. (2) Visualized medial meniscus.

gas in the location normally occupied by the cartilage. Detached portions of the cartilage may be covered with a film of opaque medium and so identified. Irregular or lineal blotchy markings on the cartilage indicate crevices or tears. Abnormal contours may indicate the presence of a cyst within the meniscus.

Figures D and E exemplify abnormalities in the synovial membrane, in this instance the outlines of a synovial hernia. Similarly, this method may serve to distinguish adhesions or intra-articular ligaments. Synovial proliferation may clearly become visualized.

COMMENT

In clinical observation of 28 patients who were examined by this method of double contrast visualization of the intra-articular structures, there was no evidence of damage attributable to the procedure. About half of the patients were operated upon after the roentgen examination was carried out and there was no macroscopic evidence that the procedure had disturbed the synovia. In one instance, tissue was studied microscopically and there was no evidence of reaction to the iodide.

490 Post Street.

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Vesicular and Bullous Diseases of the Skin

Cytologic Diagnosis

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FOR YEARS clinicians have needed an objective method for the rapid differential diagnosis of vesicular and bullous diseases of the skin. Many of these conditions, such as herpes simplex and herpes zoster, are caused by viruses. Precise methods for the diagnosis of viral diseases are provided in large medical centers, but by and large, such services are not available to physicians, elsewhere. Biopsy examination has therefore been the main diagnostic support, but that procedure is time-consuming, expensive, and occasionally disfiguring.

This communication outlines a new diagnostic technique that is superior in many ways to the methods now in use.

Tzanck^{2, 3} was the first to note that distinctive cell types could be found in scrapings from the surface of dermal lesions. His observations have been confirmed and extended by workers in this country.¹ The method outlined in this report has been developed to the point where a number of vesicular entities can be diagnosed with certainty by cytologic examination.

METHOD

The first step is to transfer epidermal cells from a dermal lesion, preferably a new one, to a glass slide with as little trauma as possible to the specimen. Although satisfactory preparations can often be made from crusted lesions, comparative studies have shown that material from an early lesion is more suitable than from a mature one and should be used if available.

To obtain the specimen the "roof" of the vesicle is reflected and the base of the lesion is blotted dry with sterile gauze. The lesion is then "pinched up" to prevent gross bleeding which would render microscopic examination of the slide difficult.

The sharp edge of a scalpel held perpendicular to the surface of the skin is then scraped firmly across the base of the lesion. One or two quick strokes is usually sufficient, since in most instances the cells are only loosely attached. The collected material is immediately transferred to a clean glass slide and spread gently with a minimum of "scrubbing." The

• A new technique, first described by Tzanck, for diagnosis of vesicular and bullous diseases of the skin by cytologic examination of material firmly scraped from lesions has a number of advantages over excision of biopsy specimens. It takes relatively little time, is painless, simple and inexpensive. The method also has value in research and teaching.

preparation is then air dried, fixed in methyl alcohol, and stained with commercial Giemsa or hematoxylin-eosin stains.

The entire operation from the incision of the vesicle to the final examination of the slide under the microscope may be performed in one hour.

A brief description of the cytologic features to be found in some of the vesicular dermatoses follows:

Herpes Zoster, Herpes Simplex, Kaposi's Varicelliform Eruption, Varicella

The cytologic features in these four diseases are similar and at present there is no way to distinguish one from the others cytologically. The consistent feature is the presence in profusion of multinucleate giant cells, some of which attain dimensions ten times those of normal epithelial cells. Viral inclusion bodies are seen especially well in herpes zoster and varicella. The "rosette" formation shown in Figure 1, D has so far been seen only in herpes zoster. The significance of this peculiar formation is not clear. A morphologic resemblance to the "L. E." cells seen in lupus erythematosus will be noted. It is possible that the rosette represents *in vivo* phagocytic activity of leukocytes against the abnormal giant epithelial cells. This formation is observed in about 20 per cent of the specimens from lesions of herpes zoster. Giant cells or rosette formations are not seen in specimens from the lesions of other viral diseases of the skin such as variola and vaccinia.

Pemphigus, Benign Familial Pemphigus, Pemphigus Erythematosus

The classic "pemphigus" epithelial cell is present in great numbers in specimens taken from the lesions of these three diseases. The cell is rounded and has an abnormally large nucleus. Peripheral "condensation" of cytoplasm, observed as a darkly stained

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basophilic margin, is a constant feature. The cells are usually arranged in a mosaic pattern and are present in profusion. No giant cells are seen.

In dermatitis herpetiformis the epithelial cells are normal, but the large number of eosinophils present suggests the diagnosis.

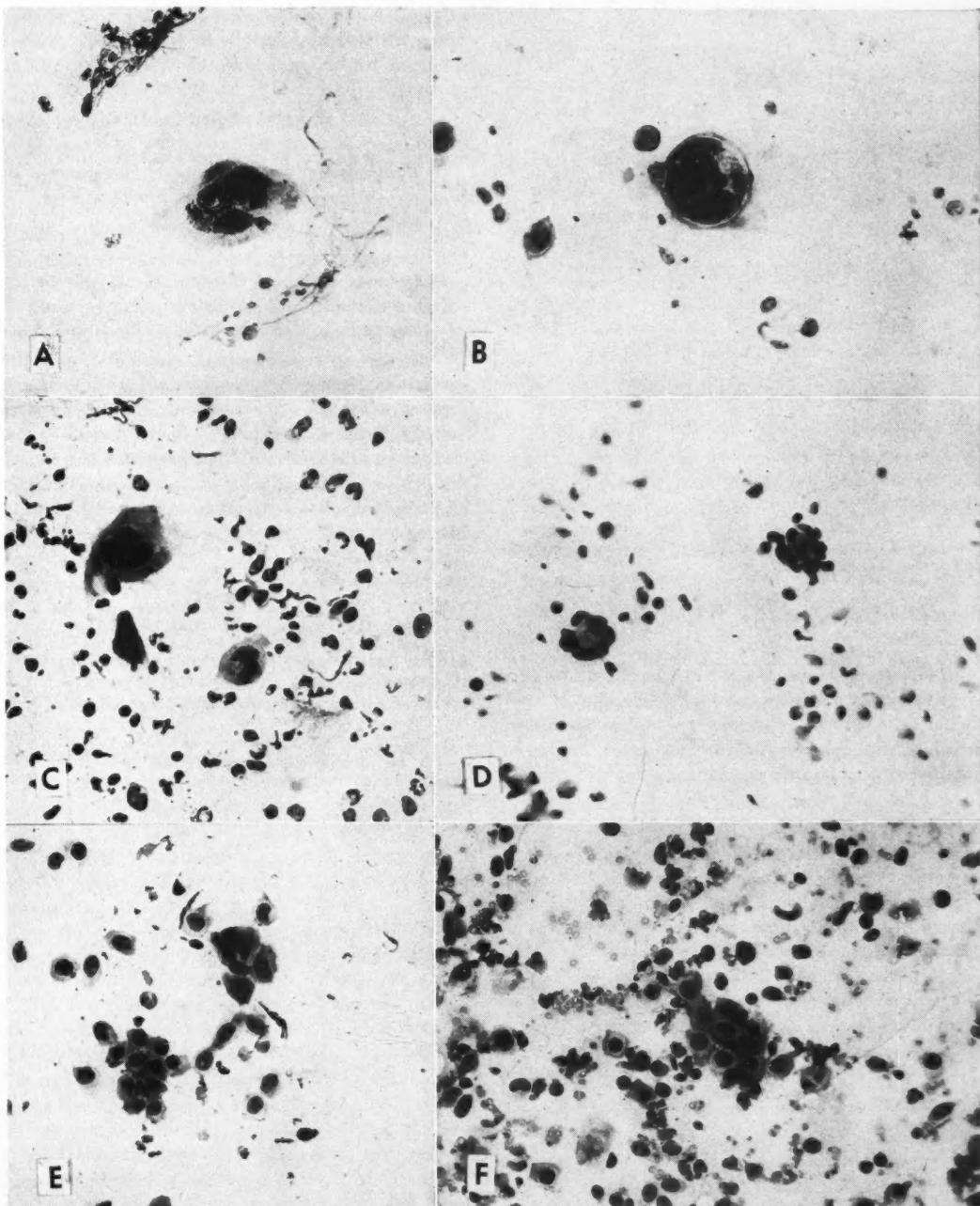


Figure 1.—*A*, Herpes simplex giant cell with intranuclear inclusion body ($\times 500$). *B*, Herpes zoster multinucleate giant cell ($\times 500$). *C*, Varicella giant cells ($\times 250$). *D*, Herpes zoster "rosettes" (giant cells being phagocytosed by leukocytes?) ($\times 250$). *E*, Pemphigus, showing a mosaic of abnormal epithelial cells ($\times 250$). *F*, Benign familial pemphigus, showing same cytologic picture as pemphigus ($\times 250$).

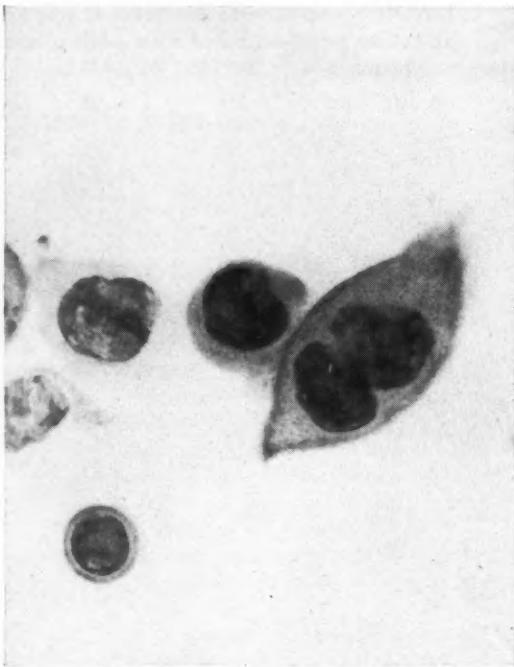


Figure 2.—Cytologic detail in the nucleus of a giant cell in herpes zoster ($\times 1,000$).

Contact Dermatitis, Burns, Primary Irritant Dermatitis.

In this group of diseases the cytologic features are large numbers of leukocytes and a few normal epithelial cells. Fibrin is usually present in moderate amounts. Polymorphonuclear leukocytes predominate in primary irritant dermatitis, whereas lympho-

cytes are more commonly seen in allergic contact dermatitis.

DISCUSSION

Although it is not suggested that the cytologic method should replace biopsy as a means of diagnosis, for vesicular lesions in which the individual cells are freely obtainable, certain advantages are obvious.

1. *Speed.* A finished preparation ready for examination may be prepared in one hour or less.

2. *Painlessness.* In ordinary circumstances, the procedure causes no discomfort to the subject.

3. *Simplicity.* Cutting and suturing are not necessary.

4. *Inexpensiveness.* Cytologic smears may be prepared at a fraction of the cost of a biopsy, and the procedure can be carried out in a physician's office.

5. *Research.* Histochemical, enzymatic and other special procedures are frequently more easily performed on cytologic preparations. The minute study of such features as inclusion body formation and nuclear and cytoplasmic detail are much more easily performed on individual cells as compared with the biopsy. Multiple preparations are easily obtained from the same lesion for teaching purposes.

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Primary Carcinoma of the Gallbladder

Review of 173 Cases

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INTEREST IN PRIMARY CARCINOMA of the gallbladder is dulled by the relative infrequency of the disease and even more because it is generally recognized to be almost incurable. Five-year cures, such as that reported by Booher and Pack,² are rare indeed. Finney and Johnson⁶ declare, "In many ways it seems hardly worth while to offer a paper on such a surgically hopeless condition as carcinoma of the gallbladder."

This gloomy situation has discouraged reports on this disease but has, on the other hand, encouraged study and speculation in an effort to arrive at better clinical results. Of chief interest to surgeons and pathologists has been the relationship of carcinoma of the gallbladder to the occurrence of gallstones, which are considerably more common in carcinoma of the gallbladder than in the general population. The possible etiological significance of this fact has intrigued pathologists and other investigators. Surgeons have considered with interest but have not agreed on whether the danger of malignant change is in itself an indication for cholecystectomy in asymptomatic cholelithiasis.

This report is based on a review of 173 cases of primary carcinoma of the gallbladder. The sources are autopsy reports from 1918 to 1948 on file at the Los Angeles County Hospital and surgical pathology reports for the years 1939 through 1947 inclusive plus the year 1949. (The surgical pathology material for the year 1948 was not indexed and hence was omitted.)

The clinical records, autopsy protocols and slides were reviewed and analyzed for pertinent data on incidence, clinical features and pathological findings. A few cases were omitted because information was insufficient or because the diagnosis seemed doubtful after review of the exhibits.

It might be mentioned in passing that, except for metastatic carcinoma, only three other malignant tumors of the gallbladder were recorded at the Los Angeles County Hospital in the period covered by this report. One of these was a primary fibrosarcoma of the gallbladder which occurred in a calculous

- One hundred seventy-three cases of primary carcinoma of the gallbladder were analyzed. In the group studied they made 2.11 per cent of all malignant tumors found at autopsy and were found in 1.89 per cent of all cases in which operation was done on the biliary tract. There was no appreciable change in the incidence of this tumor at autopsy during the period studied (1918-1948) at the Los Angeles County Hospital. Sixty-eight per cent of the cases were in females. A particularly high incidence was noted in Mexican females.

Upper abdominal pain, loss of weight, nausea and vomiting, jaundice, and palpable mass or enlarged liver were the most common clinical features. Approximately one-third of the patients in whom the lesion was found at operation and one-fifth of all the patients whose records were studied had a history of chronic gallbladder disease.

All but two of the 38 patients operated on were dead or had clinical recurrence within two years. One was alive and well 12 years after cholecystectomy.

The most common gross appearance, particularly at autopsy, was a large tumor mass replacing the gallbladder and radiating to nearby organs, particularly the liver. In about one-third of the cases the tumor was grossly limited to the gallbladder. Polypoid tumors occurred in only about 10 per cent of the cases and most of the tumors were diffusely growing adenocarcinoma. Perforation appeared in nine cases, usually with fistula to the gastrointestinal tract. All of the tumors were histologically adenocarcinoma, usually of simple glandular structure. No purely squamous cell growth occurred.

Gallstones were found in 79.8 per cent of the cases.

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Chairman's Address—Presented before the Section on Pathology and Bacteriology at the 81st Annual Session of the California Medical Association, Los Angeles, April 27-30, 1952.

gallbladder and caused death by extensive metastases. The other two were instances of lymphosarcoma and reticulum cell sarcoma involving the gallbladder as part of a widespread disease.

TABLE 1.—Incidence of Carcinoma of the Gallbladder (173 Cases)

	Autopsies	Carcinoma of Gallbladder			Operations on Biliary Tract	Carcinoma of Gallbladder	
		Cases	Per Cent of Autopsies	Per Cent of Malignant Tumors		Cases	Per Cent
Los Angeles County Hospital....	38,757	135	0.35	2.11 (all malignant tumors)	2,011	38	1.89
Collective Review of Literature by Arminski ¹	206,098	908	0.43	4.53 (carcinoma only)	46,480	569	1.22

TABLE 2.—Comparative Incidence of Primary Carcinoma of the Gallbladder Found at Autopsy (Los Angeles County Hospital, 1918-1947)

Years	Autopsies	Malignant Tumors Found	Per Cent of All Autopsies	Carcinoma, Gallbladder	Per Cent of All Tumors	Carcinoma, Pancreas	Per Cent of All Tumors	Carcinoma, Lung	Per Cent of All Tumors
		Cases		Cases		Cases		Cases	
1918-22	1,176	132	11.2	3	2.3	9	6.8	0	0
1923-27	3,496	493	14.1	10	2.0	22	4.5	21	4.3
1928-32	5,055	659	13.0	14	2.1	28	4.2	29	4.4
1933-37	9,647	1,433	14.8	31	2.2	58	4.0	83	5.8
1938-42	10,741	1,908	17.8	43	2.3	98	5.1	212	11.1
1943-47	8,632	1,759	20.4	34	1.9	68*	4.9	158*	11.3
Total	38,757	6,384	16.5	135	2.1	283	4.7	503	8.4

* 4 years only (1943-46).

No attempt to review the literature was made in connection with this report. An excellent collective review was published by Arminski¹ in 1949. He reviewed reports of 908 cases among 206,098 autopsies reported in the world literature from 1894 to 1940, and 569 cases among 46,480 operations on the biliary tract from 1891 to 1941. He added reports of 25 cases he had observed. Since then (up to February 1952) there have been seven additional reports in the American literature, reporting 193 additional cases.

INCIDENCE

Data on 135 of the 173 cases covered in this review were obtained from the autopsy reports. Those cases made up 2.11 per cent of the total number of malignant tumors found at autopsy during the 25-year period covered. The other 38 cases of primary carcinoma of the gallbladder were studied in the surgical pathology laboratory during a ten-year period. They made up 1.89 per cent of all cases in which operation was done on the biliary tract and 2.8 per cent of all cases in which cholecystectomy was carried out. The incidence observed in autopsy reports (Table 1) was considerably lower than that reported by Arminski.¹

The records of all cases of malignant tumor in which autopsy was done at the Los Angeles County Hospital from 1918 to 1947 were analyzed recently by Steiner, whose findings, both published and unpublished, have been freely drawn upon in preparing this report. The author is indebted to him for basic data essential to study of incidence and for specific observations regarding carcinoma of the gallbladder.

The quinquennial incidence of primary carcinoma of the gallbladder as observed at autopsy at the Los Angeles County Hospital for the period studied is shown in Table 2. It is compared with the findings of Steiner, Butt, and Edmondson¹¹ at the same hospital for the incidence of all malignant tumors, primary carcinoma of the lung and carcinoma of the pancreas, their figures being modified slightly to include 1947. Carcinoma of the lung is included for purposes of comparison as a tumor of increasing incidence, and carcinoma of the pancreas as a tumor which has not increased in incidence and which is clinically related to primary carcinoma of the gallbladder. This table indicates a fairly constant incidence of the disease during the period studied.

Steiner in his review of malignant tumors found at autopsy at the Los Angeles County Hospital tabulated all of the cases according to sex and race. Most patients at the Los Angeles County Hospital are of the Caucasoid, Mexican and Negroid races, 98.8 per cent of all autopsies being done in these races. Mexicans are listed separately because so large a proportion (17.4 per cent) of all autopsies at this hospital were done on persons of that race.

In analyzing the age, sex, and racial distribution for cases of primary carcinoma of the gallbladder seen at autopsy, Steiner found a notably higher rate in Mexican females than in any other group: While the corrected sex ratio of 2.88 females to 1 male reflected the known predisposition of females to this disease, the incidence in Mexican females was almost three times that in Caucasoid females. He also noted that the peak of incidence was at a lower age in Mexican than in Caucasoid females.

The distribution by age, sex, and race for the 173 cases recorded in autopsy reports and in surgical pathology reports is shown in Table 3. Of these, 118 or 68.2 per cent were in females, a proportion close to the 73.1 per cent in females reported by Arminski.¹ Table 3 also illustrates that the disease occurs more frequently in younger persons among Mexicans than among Caucasoids. Four of the seven patients under 40 years of age were Mexican females. The sex and racial distribution of the 173 cases compared with the percentage distribution of the same groups in 35,293 autopsies was as follows:

Race-Sex Group	Percentage of All Cases of Carcinoma of Gallbladder	Percentage of All Autopsies (35,293)
Caucasoid male	27.2	48.1
Caucasoid female	42.8	27.0
Mexican male	3.5	9.4
Mexican female	21.9	8.0
Negroid male	1.2	3.4
Negroid female	3.5	2.9

The unusually high incidence in Mexican females is further illustrated by the fact that carcinoma of the gallbladder comprises over 8 per cent of all malignant tumors found at autopsy in Mexican females.

CLINICAL FEATURES

Symptoms and Physical Findings

The incidence of the most common symptoms and signs in the 173 cases is shown in Table 4. Percentages are based on cases in which definite information was available. The findings are similar to those reported in the literature.

Abdominal pain when present was usually in the right upper quadrant of the abdomen and was of the colicky type in 21 per cent of the surgical pathology cases and 9.3 per cent of all the cases. The pain was variously described as dull, sharp, intermittent or continuous. Radiation to the back or right shoulder was present in some cases. The duration of pain in the surgical pathology group varied from one week to over ten years. Abdominal tenderness was present in many cases, particularly in the surgical group.

History suggestive of chronic gallbladder disease was reported for 34 per cent of the surgical group and for 22 per cent of all cases. In the collective review of Arminski¹ the incidence of past history of gallbladder disease was 52 per cent.

Weight loss, frequently rapid and pronounced, occurred in almost all cases, even those in which patients were still obese when admitted to the hospital.

Jaundice was present in 28 of the 38 surgical cases and in 108 of the 160 cases in which definite information was available. In the surgical group one patient had had jaundice for eight months at the time of operation, but in no other case had jaundice been present for more than four weeks before operation.

TABLE 3.—Age, Sex, and Race Distribution of 173 Cases of Carcinoma of the Gallbladder

Age	Caucasoid		Mexican		Negro	
	Male	Female	Male	Female	Male	Female
21-30	..	1
31-40	..	1	1	4	..	1
41-50	3	3	2	9
51-60	9	16	1	11	1	2
61-70	13	27	1	10	..	2
71-80	17	21	1	3	..	1
81-90	5	6	..	1	1	..
Total	47	74	6	38	2	6

TABLE 4.—Incidence of the Most Common Symptoms and Signs in 173 Cases of Carcinoma of the Gallbladder

Symptom or Sign	Surgical Cases		All Cases		Percent- age in Collective Review by Arminski ¹
	No.	Per Cent	No.	Per Cent	
Pain in abdomen	33	86.8	110	73.3	76.1
Weight loss	17	94.4	87	66.5	64.1
Nausea or vomiting	22	81.5	81	67.5	
Jaundice	28	73.7	108	67.5	57.7
Mass in right upper quadrant	18	58.1	76	55.9	53.2
Enlargement of liver	22	68.8	99	71.7	49.1
Tenderness	20	90.9	79	62.2	64.0
Ascites	0	0	27	20.1	20.8

Pain occurring at some time during the course of the disease was associated with jaundice in almost all cases. Painless jaundice occurred in only four of the surgical cases and in 18 of all cases.

Enlargement of the liver or a palpable mass in the upper abdomen was noted in well over half the cases. Frequently it was difficult to differentiate between a mass and an enlarged liver.

Laboratory and Roentgenographic Findings

Erythrocyte counts or hemoglobin determinations were made in 21 of the surgical cases. In eight there was no anemia; in five anemia was slight, and in seven moderate. Data available on 76 of the 135 cases in the autopsy series disclosed no anemia in 16, slight in 12, moderate in 32 and severe in 18. Most of the other laboratory studies were concerned with differential diagnosis of jaundice or evaluation of liver function. A wide range of results was recorded which do not seem statistically valuable in this study.

Because of the tendency of carcinoma of the gallbladder to destroy this organ and to form a large local mass centering about the gallbladder, and because of the frequent presence of gallstones, a high incidence of roentgenographically observable abnormalities would be expected. Cholecystograms made in 25 cases within a reasonably short time before operation or autopsy showed the gallbladder to be nonfunctioning in 24 cases and to contain stone in 8; in 2 cases examination was unsatisfactory but in no case were the findings reported as normal. In

most cases with nonfunctioning gallbladder the tumor involvement of the gallbladder was extensive, but in no case was the tumor visualized or outlined by roentgenographic appearance. A plain film of the gallbladder was made in 23 cases. In eight cases stones only were observed, in three cases a mass only, and in two both mass and stones. In ten cases no abnormality was visualized in the plain film, although at autopsy stones were found in eight cases and in several there were tumors large enough to extend beyond the gallbladder. In roentgenographic studies of the gastrointestinal tract abnormalities resulting from pressure or invasion by tumor were frequently observed. These were late findings but in some cases were helpful in diagnosis, while in others they were misinterpreted as indicating that the gastrointestinal tract was the site of the primary tumor. The change most frequently present was duodenal deformity; other frequent findings were abnormalities in the stomach and large bowel. Cholecystoduodenal fistula was observed in only one case.

In a number of the reports in the literature cases have been classified according to the dominant or composite clinical impression, a more graphic presentation than tabulation of symptoms and signs. The cases in this study have been considered in this way, by a classification modified from Boyce and McFetridge:³

a. Cases with recent symptoms and signs of gallbladder disease, but with no evidence to suggest malignant disease	13
b. Cases with past and recent symptoms and signs of gallbladder disease with no evidence to suggest malignant disease	11
c. Cases with recent history of gallbladder disease and recent symptoms and signs of malignant disease.....	34
d. Cases with past symptoms and signs of gallbladder disease and evidence of malignant disease.....	24
e. Cases with evident malignant change and no symptoms or signs of gallbladder disease.....	47
f. Cases with no evidence of malignant or gallbladder disease	14
g. Cases with obstructive jaundice as principal clinical feature	17
Painless jaundice	8
With pain, usually in right upper quadrant, and often a mass.....	9
(Jaundice was also present in 19 additional cases in Groups a and d.)	
h. Cases in which information was inadequate	13

Only 35 patients had a history of chronic gallbladder disease while 60 patients had no symptoms of gallbladder disease.

Clinical Diagnosis and Course

The clinical diagnoses made in the 38 cases in the surgical group were as follows: Cholecystitis or cholelithiasis, 10; obstructive jaundice, 10; carcinoma of the pancreas, 6; carcinoma, site not specified, 4; carcinoma of the bowel, 3; carcinoma of the gallbladder, 3; hepatitis, 2.

The most common diagnosis in the 135 cases in the autopsy group was that of intra-abdominal malignant disease, made in 75 cases—carcinoma of the stomach in 20, of the pancreas in 16, and of the gallbladder in 13.

The correct diagnosis was made before operation or autopsy in only 16 of the 173 cases, a proportion similar to that reported in the literature. There was no constant clinical pattern in these cases. There was a definite history of gallbladder disease in five cases and of painful jaundice and a palpable mass in several. Correct diagnosis was made before operation in three patients. One of them was a Negro woman 62 years of age who entered the hospital because of constant pain, a mass in the right flank, and loss of weight. She had had gallbladder drainage for stones three years previously. The second was an obese Mexican woman 60 years old who was admitted to the hospital in an attack of colicky pain in the right upper quadrant of the abdomen and a palpable mass; she had had chronic cholecystitis with intermittent colic for fifteen years. The third patient was a 73-year-old white woman who for a short time had had jaundice and pain in the area of the gallbladder, radiating to the shoulder, and a palpable firm mass in the right upper quadrant of the abdomen.

It is noteworthy that pain was present in five of the six surgical cases diagnosed before operation as carcinoma of the pancreas and in all ten cases diagnosed before operation as obstructive jaundice.

In the autopsy group symptoms preceded death by less than a year in 60 cases, and operation was attempted in only 20, in 14 of which the tumor was inoperable and death ensued within a year. In one patient extensive resection of the gallbladder, duodenum and colon was done; the patient died of postoperative shock and widespread metastases were found at autopsy. Cholecystectomy was done on four patients, two of whom died in the immediate post-operative period, one with metastases which were found at autopsy. The other two died of metastases in four weeks and in 17 months respectively.

The clinical course of the 38 surgical cases was equally poor:

Duration of Symptoms	Cases	Cases with Metastases Found at Operation
Less than 1 month.....	12	9
1 to 6 months.....	17	15
12 to 18 months.....	3	3
18 to 24 months.....	1	1
2 to 5 years.....	3	1
Unknown	2	0

The operative procedures done in these patients were: cholecystectomy (23); cholecystostomy and biopsy (2); exploration and biopsy (11); cholecystoduodenostomy and biopsy (1); cholecystogastrostomy and biopsy (1).

TABLE 5.—Incidence of Gallstones in 173 Cases of Carcinoma of the Gallbladder

Age	Number of Cases	Number with Gallstones	Per Cent with Gallstones	Location of Stones			
				Gallbladder	Cystic Duct	Hepatic Ducts	Common Bile Duct
21-30	1	1	100.0	1	0	0	0
31-40	6	4	66.6	4	0	0	1
41-50	17	13	76.4	13	1	0	0
51-60	40	34	85.0	33	4	0	4
61-70	53	44	83.0	42	5	1	8
71-80	43	33	76.7	30	2	0	8
81-90	13	9	69.2	9	1	0	1
Total	173	138	79.8	132	13	1	22

The known postoperative survival of this group was as follows:

Operative deaths	4 (3 with metastases)
Less than one month	6 (all died)
1 to 6 months	15 (all with metastases; 11 died)
6 months to 1 year	4 (3 with metastases; 2 died; 1 living and well, no further follow-up)
1 to 2 years	6 (5 with metastases; 3 died; 1 living and well, no further follow-up)
2 to 5 years	0
Over 5 years	1 (last seen Nov. 1951 5 years and 3 months after operation; had lost 30 pounds of weight, and has many cardiac and gastrointestinal complaints)
Over 10 years	1 (alive and well 12 years after operation)
Unknown	1

Thus of all patients followed all but three were dead or had recurrence within two years and only two were known to be alive after five years. One of these, the youngest in the group, was 24 years old at the time of operation and is in good health after twelve years. Her symptoms and the findings were those of acute cholecystitis and the tumor was found unexpectedly.

PATHOLOGICAL ANATOMY

Gross Pathology

There are several important components of the gross pathologic changes relative to carcinoma of the gallbladder. These are the appearance of the tumor itself, the changes produced in the gallbladder by the tumor or from preexisting disease, and the nature of the extension and metastases.

In almost all instances the disease was far advanced at the time of operation or autopsy. Examples of early lesions were rare. There were only eight cases in which the tumor was not observed until microscopic study was carried out; in those cases the growth was limited to the mucosa or wall of the gallbladder. Even in those cases, with one exception, the disease had already metastasized and later caused death. In a few instances the tumor was limited to one portion of the wall of the gallbladder,

producing a nodule, plaque or small polypoid tumor. In most instances the growth filled the lumen (except for stones) or replaced the wall, frequently with direct extension into adjacent structures, particularly the liver. Polypoid tumors occurred in only 21 of the 173 cases.

The tumor was grossly limited to the gallbladder in 62 cases, the gallbladder being shrunken and contracted in 23 cases, of normal size in 29, and distended or enlarged in 19.

Most frequently the gross appearance was that of wide local growth radiating from the gallbladder into the nearby organs, particularly the liver. Such a large local tumor was present in this series in 106 cases, in most of which the gallbladder was itself small or normal in size; it was enlarged or distended in only 12 cases. In 32 cases the gallbladder was destroyed by tumor; often only remnants remained within the mass, identifiable only by the cluster of stones frequently present. The formation of a large local mass was frequently detectable by physical examination and in some cases by roentgenographic studies.

Perforation occurred in nine cases. In six of them a fistula was formed to the gastrointestinal tract, and in three there was generalized peritonitis (bile peritonitis in one case). In two cases local abscesses were present.

The bile ducts were involved by direct extension in 81 cases (47 per cent), the common bile duct in 44 of these. In some cases the growth followed the bile ducts and could be distinguished from primary carcinoma of extrahepatic bile ducts only with difficulty if at all.

In addition to the local mass in the liver there were disseminated metastatic nodules in 80 cases. Regional lymph node metastases were described in 84 cases (49 per cent). Less frequently involved in metastases were the peritoneum (43 cases), the gastrointestinal tract (41), the pancreas (23), lungs (10), bones (6), kidneys (6), adrenal glands (6), the portal vein (6), the superior vena cava (2), ovaries (5), pleura (5), abdominal wall (3), diaphragm (3), spleen (2), pericardium (1), and myocardium (1).

The most common associated pathologic condition was gallstones, which occurred in 138 or 79.8 per cent of the cases (Table 5). Stones were also present in the bile ducts in 36 cases, in the common bile duct in 22. As the disease was usually in a late stage when observed and the organs diffusely infiltrated, it was difficult and often impossible to find gross evidence of preexisting cholecystitis. Hydrops or empyema of the gallbladder was present in only three cases.

Other associated diseases were abscess of the liver or suppurative cholangitis (five cases), double primary carcinoma (six cases—two of the prostate, two of the uterus, one of the colon, and one of the ovary) and diabetes (six cases).

There were only six cases in which carcinoma of the gallbladder was an incidental finding and not a major cause of death.

Microscopic Pathology

All the tumors in the series were adenocarcinomas. The histological types were as follows:

Simple glandular adenocarcinoma.....	110
Undifferentiated adenocarcinoma.....	24
Anaplastic carcinoma.....	19
Carcinoma simplex.....	5
Colloid (mucoid) carcinoma.....	5
Scirrhous carcinoma.....	4
Papillary carcinoma.....	2
Mixed types of adenocarcinoma.....	22
Mixed squamous and adenocarcinoma.....	6

There were no cases of pure squamous cell carcinoma in the series. The most common histologic type was simple glandular carcinoma infrequently having a slight resemblance to gallbladder epithelium. More often the cellular structure resembled that of carcinoma of the gastrointestinal tract. There were no early lesions which could be studied for histogenesis. In the few cases in which involvement could be observed only microscopically the tumor was fairly advanced. In two cases the appearance of the tumor was suggestive of carcinoma *in situ*; in both the tumor was in the mucosa and in the epithelium of the Rokitansky-Aschoff sinuses. No epithelial metaplasia was seen in uninvolved epithelium.

In most cases the widespread tumor growth in the wall of the gallbladder had obliterated any evidence of preexisting chronic cholecystitis. However, in almost all cases where portions of wall were still present and uninvolved by tumor, chronic inflammatory changes including fibrosis were present.

RELATIONSHIP TO CHRONIC CHOLECYSTITIS AND CHOLELITHIASIS

It is generally held that chronic cholecystitis precedes carcinoma of the gallbladder in most cases. There was little opportunity to study this relation-

ship in this series because the disease was advanced in most cases. However, in most instances where it could be studied there was evidence of chronic inflammation or fibrosis, although histogenesis and the preexistence of nonmalignant alterations in the epithelium could be observed in only a few cases. In two cases histological findings suggested adenoma malignum or carcinoma *in situ*. In many of the cases in which malignant growth was far advanced, areas of uninvolved mucosa could be found, and in these areas the epithelium was normal.

Cholelithiasis was present in 138 or 79.8 per cent of the 173 cases (Table 5). Arminski¹ reported an incidence of 73 per cent in his collective review of the literature. Most observers believe that the stones, like the inflammatory changes, antedate the tumors, and some have suggested that the stones are an important causative factor. This has led to attempts at production of carcinoma of the gallbladder in experimental animals, usually guinea pigs, by placing human gallstones and other substances within the gallbladder. Desforges and co-workers⁵ in a recent report indicated that the results, particularly with gallstones, were either negative or inconclusive.

It is well known that gallstones occur more frequently in females than in males. Data on age and race differences are not as abundant but in general the incidence increases with age in both sexes and is lower in the Negroid than in the Caucasoid races. Among persons with carcinoma of the gallbladder the incidence of stones is greater than in the general population and is also greater proportionately for males and for Negroid persons. This incidence suggests that if gallstone antedates the development of carcinoma it may be a predisposing factor, although it must be remembered that gallstones are quite common, particularly in older persons, while carcinoma of the gallbladder is rare.

If gallstones are in some way related to the development of carcinoma of the gallbladder, some parallelism in age, sex, and racial distribution of the two conditions might be expected, although this incidence may, of course, be purely coincidental, as in the increase of incidence with age. According to available statistics, as in the recent report of Lieber,⁹ the incidence of gallstones is highest in Caucasian females and lowest in Negro males. Similar variations are to be noted in data on carcinoma of the gallbladder. According to figures from the Los Angeles County Hospital for the period 1918 to 1937, the incidence of gallstones found at autopsy was 4.4 per cent, but no breakdown as to age, sex, race or fatal outcome is available for the period covered by this report. For the years 1934 through 1937, the incidence of gallstones in 8,158 autopsies on persons

over 10 years of age was 6.3 per cent. Distribution by race and sex was as follows:

Race	—Per Cent of All Autopsies—	
	Male	Female
Caucasoid	4.7	8.6
Mexican	3.8	9.8
Negroid	3.6	4.1

Although the incidence of gallstones is greater in females than in males, with the greatest sex difference in the Mexican race, there is only a slightly greater incidence of stones in Mexican females than in Caucasoid females. Among younger females, however, the racial difference is greater: In 19,908 autopsies the incidence of gallstones in Mexican females under 40 years of age was 29 per cent, while in Caucasoid women of the same age the incidence was only 8 per cent.

As previously mentioned, the very poor results of treatment for carcinoma of the gallbladder have led some observers to advocate prophylactic cholecystectomy in any patient who has gallstones, even if there are no symptoms. Others point out that gallstones are so common in middle age and later life and the incidence of carcinoma of the gallbladder so low that the operation would entail a greater risk than the disease. Some of the differences of opinion arise from variations in reported incidence of gallstone and, to a lesser extent, of carcinoma of the gallbladder, particularly in reports based on examination of surgical specimens.

It is of little or no value to quote statistics on average or total incidence of gallstones because of the wide variations in sex and race. Reports of large series of cases analyzed by age, sex, and race, as in the recent excellent report by Lieber,⁹ are needed. Comparable statistics on carcinoma of the gallbladder

are also needed but are difficult to obtain in large numbers. Additional studies of experimentally induced tumors of the gallbladder, as well as histological studies of early lesions, should also be of value in the problem of the relationship of cholelithiasis to carcinoma of the gallbladder.

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Does Your Hospital Need a Recovery Room?

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THE IDEA of a special room or ward in which patients can recover from operative anesthesia is not new but has recently been revived. The advantages claimed for a recovery room are that in the immediate postoperative period all patients who need it can have the care of specially trained nurses without delay; that equipment and supplies needed in such care are readily available in one area and need not be duplicated elsewhere; that more patients can be operated upon and released the same day, after recovery; that emergency operations can be done at any hour without disturbance to patients or routine in other wards; that ward nurses would be relieved of the care of patients at the time when nurses are busiest and the patients need most attention, and that nurses caring for recovering patients need not be hampered by visitors to these patients or to others on the ward.

All who have had experience with a recovery room—surgeons, anesthetists and nurses—are enthusiastic about the results. There are problems, however in setting up a recovery room near the operating rooms in space already used for other purposes, and even in new construction the general idea of a recovery room must be applied in terms of probable need. To determine both the desirability of a recovery room and the particular needs which it would fill, a survey was made of surgical cases in a 220-bed hospital with seven to eight operating rooms which is in an urban area near Los Angeles. The object was to learn what patients would have been cared for postoperatively in a recovery room had one been available.

During the period of the survey there were 32 working days including six Saturday half-days. A total of 574 patients were operated upon. Of the total, 99 had operations for which recovery room care is not considered ordinarily necessary—cesarean section, adenotonsillectomy and outpatient treatment. Of those patients who might have been sent to a recovery room, 180 (38 per cent) were males and 295 (62 per cent) females.

To make possible a judgment as to which patients would have been sent to a recovery room, a chart was placed on each floor for recording of the recovery time and the condition of each of the 475 pa-

• *In a survey made to estimate the need for a special room in which patients could recover from anesthesia after operation, it was found that of 475 cases in which this service might have been used, it would have been desirable in 296; that recovery room care would probably have relieved ward nurses of the duty of special care during their busiest hours; that recovery room care was indicated in a high percentage of cases in which certain anesthetics were employed, and that the need for recovery room care appeared to increase in proportion to the amount of pre-sedation given.*

tients. The author then correlated the information on these charts with the nurses' other records. The conclusion was that 296 patients would have been sent to a recovery room; of these, 111 (37.5 per cent) were males and 185 (62.5 per cent) females, a proportion very close to that for all cases in the survey and one to be considered in the planning of this facility. The distribution on wards was as follows:

Type of Ward	Cases in Survey	"Recovery Room Cases"	Per Cent
Medical	53	32	60.4
Pediatric	22	16	72.7
Neurosurgical	46	31	67.3
Surgical	354	217	61.0
	475	296	62.3

It might be noted here that had a recovery room been available the equipment, supplies and nursing services needed for the patients during recovery time would have been combined rather than distributed or duplicated through eight wards. Of these factors, of course, the most important is the service of specially trained nurses. Special nurses cared for 48 of the 296 "recovery room patients"; had these patients in fact been concentrated in a recovery room all would have been under the care of special nurses during the critical period.

One factor affecting both efficiency of nursing service and the care available for patients after operation is the time at which the patients arrive on the ward. This time was noted for all patients in the survey and the information was grouped for three periods in the day. The first period is before 11:30 a.m., the hour at which all nursing and aide person-

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nel are occupied in serving lunch. It is before this hour that floor nurses are busiest in discharging patients, making rounds with physicians, and helping with dressing trays and personal care of patients. The second period, from 11:30 to 1 p.m., is that in which nurses are either at lunch or helping with feeding problems. The third period is after 1 p.m.

Period	Patients Returned to Ward During Period	Patients Who Would Have Gone to Recovery Room No.	Per Cent
Before 11:30 a.m.....	265	159	60.0
11:30 to 1 p.m.....	120	82	68.3
After 1 p.m.....	90	55	62.3
	475	296	62.4

It is observed from these figures that the greatest number of patients arrived during the period in which routine duties are heaviest and that of those arriving during the lunch period the greater proportion would have gone to a recovery room had there been one. It is to be noted that the recovery time for some patients arriving before 11:30 a.m. extended well beyond that time. Average recovery time for "recovery room patients" was 1 hour and 45 minutes.

Several factors were studied which might aid in establishing indications for sending patients to a recovery room. One of these was the kind of anesthetic used. The following list shows the percentage of "recovery room patients" among those receiving one of the seven anesthetics most commonly used in the cases in the survey (excluding local anesthetics):

Anesthetic	Number of Cases in Which Used	"Recovery Room Patients" Number	Per Cent
Pentothal-spinal	89	53	60
Pentothal-curare-gas-oral tracheal	76	73	96
Pentothal-gas	65	48	74
Pentothal-curare-gas	54	48	89
Spinal	46	2	4
Pentothal	45	27	60
Pentothal-spinal-gas	20	14	70

That pre-sedation affects recovery time is indicated by the facts that of 22 patients who were not given pre-sedation, only eight or 36 per cent would have been sent to a recovery room; of 59 patients given light pre-sedation, 32 or 54 per cent; moderate (258 cases), 162 patients or 63 per cent; and heavy (136 cases), 94 patients or 70 per cent.

NOTE: Since the presentation of this paper a new and extensive review and bibliography has been published. The author will be happy to help anyone interested in a review of a hospital in determining its need for a recovery ward.

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Discussion by WILLIAM H. MORAN, M.D., La Canada

Dr. McIntosh has, I believe, clearly demonstrated in his analytical study the importance of a postoperative area, whether it be a room, a ward, or a concentration of patients on a floor or in a hospital wing. The value of such a service to the patient, the hospital, the surgeon, and the anesthesiologist is evident from these statistics.

I would like to recount, briefly, my own experience. Nine years ago in an Army general hospital of 3,000 beds, the anesthesia service was confronted with an alarming increase in postoperative complications. At one time there were 11 cases of atelectasis in the surgical wards. These cases were occurring with all types of anesthesia, and in all types of surgery.

As in private hospitals today, we had a shortage of nurses. A recovery ward was placed immediately adjacent to the surgery. Both the nursing and enlisted personnel were given intensive training in the postoperative care of patients by members of the surgical service and the anesthesia service. All available equipment for treatment and prophylaxis was pooled in the recovery ward.

The incidence of surgical and anesthetic complications promptly dropped and remained within a normal rate during the next year. All surgical patients, except those receiving minor surgery with local anesthesia, were placed in this ward. All were removed to their respective surgical wards as soon as possible, after consultation between the surgical service and the anesthesia service.

Carcinoma of the Prostate

Diagnosis and Treatment

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CARCINOMA OF THE PROSTATE is the second most common cancer in men. In 1934 Arnold Rich,¹⁵ a young pathologist, announced in a now well known paper read at a clinical meeting of the American Urological Association in Baltimore, that the incidence of cancer of the prostate in men past the age of 70 was 28 per cent. This caused the audience, many in it approaching that age, to take heed. Rich went on with the reassurance that the majority of persons in that age bracket who had prostatic cancer did not die of it; in fact most such lesions were not even diagnosed clinically—just as Fate would later have it in the case of probably the most outstanding urologist of our times. Whereas previously the prostate had been too often ignored in routine autopsies, thereafter it drew the attention of many pathologists throughout the country, who corroborated Rich's revolutionary observation.

As a rule diagnosis of carcinoma of the prostate is not difficult when the lesion is in advanced stage. The early symptoms of cancer of the prostate cannot be differentiated from those of any other obstruction of the neck of the bladder. They are well known to all physicians: hesitancy, diminution in the size and force of the urinary stream, nocturia and dysuria. The disease is often asymptomatic, and the initial symptoms may be those caused by perineural and bony metastases: backache and pain radiating down one or both legs, accompanied frequently by edema at the ankles.

The most important step in the diagnosis of cancer of the prostate is the rectal examination. In the early stage the tumor is palpated as a nodule of third degree induration in an otherwise fairly homogeneous gland with a smooth capsule. Extension throughout the prostatic capsule, periprostatic tissues, seminal vesicles, the membranous urethra, and the bladder results in fixation of the gland so that it cannot be freely moved from side to side. The gland becomes very hard and irregular, much more so than with tuberculous or non-specific prostatitis. Stones in the prostate, when palpable, will often yield the sensation of crepitus and are frequently seen on x-ray examination.

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• About 28 per cent of men between the ages of 71 and 75 have cancer of the prostate. Many of them do not die of the disease, but with the life span ever increasing, this problem is becoming more important.

In the early stages the condition is asymptomatic; when the symptoms of urinary obstruction arise, the cancer is usually too advanced for cure. Cure depends on early diagnosis and, therefore, on routine rectal examination. The solitary hard nodule of early prostatic cancer becomes a stony hard fixed prostate as the condition progresses. X-ray and acid phosphatase studies are of help only after the cancer has metastasized. As many as 50 per cent of patients with rectally palpable early carcinoma of the prostate can be cured by radical perineal prostatectomy. Often, simple enucleation or transurethral resection is sufficient to effect cure in the case of occult carcinoma. However, some observers believe that when cancer is detected by microscopic examination of a prostate that has been removed, a radical operation should be done as soon after the initial operation as feasible. Early orchidectomy and estrogen therapy are of considerable help in slowing the process of advanced prostatic cancer and may postpone the need of transurethral resection to relieve obstruction. When these measures fail, bilateral adrenalectomy, cortisone therapy, pituitary irradiation, and pituitary extirpation have been employed, with moderate success, in an effort to diminish the androgen level.

In most cases the osseous metastasis of carcinoma of the prostate can be demonstrated in kidney-ureteral-bladder roentgenograms. Osteoblastic metastases and less commonly osteolytic metastases are most frequently found in the lumbar spine, pelvis and the neck of the femur. Later the ribs and other bones become involved. Paget's disease sometimes simulates the picture of bony metastases. An elevated alkaline phosphatase which is found in both conditions and simply indicates osteoblastic activity will ultimately drop after therapy with estrogens in the case

of carcinoma of the prostate, for estrogens have a beneficial effect on cancer but none in Paget's disease.

Despite the history, physical examination and x-ray studies, the diagnosis of carcinoma of the prostate may sometimes still be uncertain. Huggins^{5, 7, 8} in his classical work in 1941 demonstrated the co-existence of elevated acid phosphatase and carcinoma of the prostate after it had metastasized. Formalin-resistant acid phosphatase is an enzyme produced exclusively by adult epithelial cells of the prostate. With increase in the amount of prostatic tissue in the body, as by metastasis, there is often a concurrent rise in the acid phosphatase of the blood stream. However, since 1941 some of the enthusiasm for this test as a diagnostic aid for carcinoma of the prostate has been lost, for frequently in cases of extensive carcinoma of the prostate the acid phosphatase level is normal. It is significant, therefore, only when it is elevated, and then useful only to follow the activity of the cancer rather than to diagnose it.

The technique of Papanicolaou as applied to cell study of prostatic secretions for the detection of cancer¹ was originally heralded with enthusiasm. Malignant cells, especially those of the more differentiated prostatic cancers, are indistinguishable from normal cells and cells which have undergone metaplasia from infarcts and endocrine therapy.¹⁴ Most urologists have rejected this test in their armamentarium for the diagnosis of cancer of the prostate.

Biopsy is of considerable value in the diagnosis of early prostatic cancer. This can best be accomplished through perineal exposure, for early palpable lesions arise in the posterior lamella, which is beyond the operative range of the transurethral² or suprapubic approach. A frozen section is made at the time of exposure. It must be remembered, however, that frozen sections are notoriously unreliable, and if the operative exploration is strongly suggestive of cancer, even though the frozen sections may be reported negative, carrying out the radical operation is obligatory. Usually, however, when the frozen section is reported negative it is wiser to postpone the operation until the permanent sections are examined. The present technique of needle biopsy, which is a blind procedure, is of very little value, for the chances of securing a sample from the questionable area are slim indeed.

It must be concluded, therefore, that in early carcinoma of the prostate the most important single step is rectal examination. A clinician should be able to make the diagnosis of prostatic cancer in 90 per cent of cases. When there is doubt (it must be acknowledged that doubt sometimes arises in early cases) and in the absence of confirmatory evidence from the various diagnostic aids, the author believes

that watching the progress of the lesion over a period of two to three months without treatment is justified. If there is no regression or if there is an increase in the size of the lesion, perineal exposure and biopsy are mandatory.

Cancer of the prostate can be cured with the radical perineal or retropubic operation only when diagnosed early in its course.¹⁰ Unfortunately, usually by the time urologists observe the patients the condition has progressed to such a stage that only palliative treatment is possible. At the Brady Institute, Jewett⁹ found that of patients with extraprostatic extension of the cancer practically all who had a radical perineal operation had recurrence in six to nine years. Of those with no macroscopically detectable extension beyond the prostate, over half lived at least five years and many longer with no sign of recurrence; and the patients in this group who had recurrence in a shorter time had microscopically observable extension beyond the prostate at the time of the operation. The chance of cure, therefore, is greater if the fascia surrounding the seminal vesicles as well as the vesicles is removed. With radical perineal prostatectomy there is at least a 50 per cent chance of cure in early cases of carcinoma of the prostate.

There are certain very definite criteria for the selection of a patient for radical perineal prostatectomy.¹⁵ Certainly well less than 10 per cent of patients with cancer will meet all of the criteria. The patient's age should be such that his normal life expectancy irrespective of the cancer is greater than the expected survival with hormonal treatment. A man between 70 and 74 can expect to live seven to ten years. It is only an overzealous surgeon with a nebulous conception of his duties, therefore, who will subject a man older than 75 to the increased morbidity and mortality that go with radical perineal prostatectomy. Metastases and extension beyond the prostate, even if it shrinks with estrogens, are contraindications. The operative mortality for radical perineal prostatectomy in the best clinics is 3 to 5 per cent. Certainly the few instances of incontinence and stricture formation are a small price to pay for cure, but let no one be led to believe that the radical operation is as innocuous as simple prostatectomy.

Recently Westerborn¹⁶ of Sweden advocated cystectomy along with radical perineal prostatectomy and implantation of the ureters in the bowel. He performed a combined abdominal perineal extirpation. Whether this radical treatment is more efficacious in cancer cure remains to be seen.

If, because of the age and condition of the patient or the extent of the lesion, a radical operation is not feasible, palliative treatment should be instituted. The great majority of patients with cancer of the prostate fall into this category. Hormonal treatment

has definitely increased the longevity of most such patients. Nesbit and Baum¹² in an extensive survey in 1950 observed that patients who respond at all to hormonal therapy (and about 85 per cent do) survive longer and in greater comfort than those who do not obtain hormonal therapy. In the absence of metastases, a combination of orchidectomy and estrogen therapy had a statistically significant advantage over either therapy alone (see Table 1). In the presence of metastases, the combined therapy of orchidectomy and estrogens definitely prolonged the survival rate whereas estrogen therapy alone had little advantage over the untreated group (see Table 2).

Urologists are still at variance as to the optimum time for orchidectomy, some preferring to reserve it as a last weapon for the control of pain. Orchidectomy is far more valuable as an aid in arresting the growth of the neoplasm than as a pain-killer and should, therefore, be performed as soon as the diagnosis of cancer of the prostate is made. Not infrequently endocrine treatment alone will cause enough shrinkage of the prostatic cancer to relieve obstruction of the neck of the bladder and thus obviate the need for a transurethral resection for an appreciable period.

The problem of endocrine therapy is by no means simple or completely understood. From Huggins' and Deming's experimental work (and from personal observation) it is known that female sex hormones usually benefit and male sex hormones usually aggravate prostatic cancer. It has been observed clinically that after a variable period of time the beneficial effects of orchidectomy and estrogen therapy seem to diminish. Paralleling these findings, it has been found that the 17-ketosteroids in the urine, which represent a part of the end metabolites of the androgenic steroids elaborated by the adrenal glands and the testes, diminish after orchidectomy. Later there is an increase of the 17-ketosteroids for prolonged periods, which is attributed to stimulation of the adrenal androgens by the pituitary. Adrenalectomy or cortisone therapy causes a secondary fall in the 17-ketosteroids. Actually it has been demonstrated histologically that atrophy of the adrenal occurs with cortisone therapy, whereas corticotropin (ACTH) causes adrenal hypertrophy. Elimination of adrenal androgen activity can thus be accomplished in various ways. Huggins attempted bilateral adrenalectomy^{4, 6} in 1945 but, lacking replacement therapy, could not keep the patients alive. Today, however, this operation is carried out with a considerable degree of success by use of hormones influencing electrolyte balance and carbohydrate metabolism—desoxycorticosterone acetate and cortisone. Whether adrenalectomy will appreciably prolong the lives of patients with cancer who survive the operation remains to be seen. Cortisone has been

TABLE 1.—Five-year Survival of 597 Patients with Prostatic Cancer Without Metastases*

	Number	Per Cent Survived
Control	273	10.0
Treatment:		
Diethylstilbestrol	63	29.0
Orchidectomy	183	31.2
Diethylstilbestrol and orchidectomy.....	78	43.6

* After survey of Nesbit and Baum.

TABLE 2.—Five-Year Survival of 494 Patients with Prostatic Cancer with Metastases*

	Number	Per Cent Survived
Control	231	6.0
Treatment:		
Diethylstilbestrol	52	9.7
Orchidectomy	176	21.6
Diethylstilbestrol and orchidectomy.....	35	20.0

* After survey by Nesbit and Baum.

used with success to suppress the adrenal androgens in the adrenogenital syndrome. This occurs by inhibiting the intrinsic adrenocorticotrophic hormone of the pituitary. Investigators throughout the country are working with this theory in advanced cancer of the prostate. Scott in Baltimore has gone one step further with pituitary extirpation. Preliminary reports, however, are not too encouraging. Pituitary irradiation¹¹ seems more feasible, but the technique and the time relationship to orchidectomy and estrogen therapy have not been fully worked out. Thus at present there are four methods of reducing the adrenal androgen activity: bilateral adrenalectomy, cortisone therapy, pituitary extirpation, and pituitary irradiation.

The question of estrogen therapy and dosage is closely allied with the foregoing. In experiments on animals it has been noted that hyperplasia of the adrenal glands occurs with estrogen therapy. Smith and co-workers¹⁷ reported that TACE (chlorotriamisene), a synthetic estrogen, causes a minimum of adrenal hyperplasia, and for that reason use of that hormone has been advocated. It may be that large doses of estrogens cause an excess of intrinsic adrenocorticotrophic hormone and thus increase the androgenic activity of the adrenal glands. Repeated 17-ketosteroid determinations for each patient with prostatic cancer may provide a gauge as to optimal estrogen dose at all times. Perhaps a combination of orchidectomy, estrogens, and cortisone to depress the adrenal androgens may turn out to be the palliative treatment of choice.

Bilateral adrenalectomy and pituitary irradiation and extirpation have not yet reached the point where they are feasible clinically. Mention should be made, however, of the sometimes beneficial effects of deep

x-ray to the bones when hormonal therapy does not control the pain from bony metastases.

A problem in connection with operations upon the prostate is that of occult carcinoma—clinically unsuspected and not detected until examination of microscopic section following simple prostatectomy reveals cancer within the adenoma. Kahler¹⁰ and Moore took exception to the old idea that prostatic cancer practically always arises in the false capsule; they noted that in almost 50 per cent of cases the lesion arose in the lateral lobes and later spread to the posterior lobe. This may be the reason for Thompson's and Nesbit's¹³ success with simple prostatectomy in occult carcinoma. However, the author is inclined to agree with Hinman³ and Leadbetter who expressed the opinion that radical perineal prostatectomy should be carried out. There are yet no statistically significant data to determine which treatment should be employed in occult cancer of the prostate.

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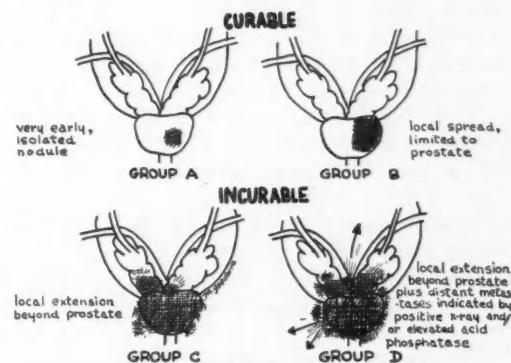
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Discussion by WILLARD E. GOODWIN, M.D., Los Angeles

Dr. Presti is to be commended for a scholarly review and synthesis of present knowledge concerning prostatic cancer.

I should like to emphasize the most important point he has made. Early prostatic cancer, like any other *early* neoplasm, is curable. In evaluation of patients it is important to perform a careful rectal examination and to attempt to discover



patients with early cancers (see groups A and B, in illustration). This clinical suspicion can and should be confirmed by biopsy. When rectal examination and biopsy prove the presence of curable prostatic cancer, radical prostatectomy should be done. When the patient is found to have incurable cancer (groups C or D) the treatment of choice (on the basis of available statistics) is prompt orchectomy and estrogen therapy.

Controversial Problems in Adenotonsillectomy

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THE REMOVAL of tonsils and adenoids, the most frequently performed operation, has been undergoing considerable criticism from many quarters in the past few years. Much of the unfavorable comment has come from physicians who believe it may cause psychic damage or increase the hazard of bulbar poliomyelitis. Some disfavor originates because of an assumption that the tonsils and adenoids have a value in the establishment and maintenance of an immunity to upper respiratory infections. By misassociation of ideas in the mind of the public, brought about by the undesired publicity of this criticism, the operation has been given an undeserved black eye.

Persons who are not physicians have a great tendency to accept any medical remark as gospel. Controversy, unfortunately, is too often brought to their attention. They become aware of the arguments, which are so necessary to the profession, and are confused. They are fearful and do whatever they can to avoid an operation. Now and then needlessly severe repeated infections or permanent disabilities of the ears, nose, throat or jaws are suffered. At times, patients are driven to supposedly less dangerous, but actually more harmful therapeutic procedures, including electrode desiccation, tonsillotomy, or x-irradiation, any of which may well seal in infection.

INDICATIONS FOR ADENOTONSILLECTOMY

The purpose of this communication is to consider only the most controversial aspects of the problems confronting adenotonsillectomy today. There is little to substantiate theories that tonsillar function plays a part in blood formation or in the production of immunity. Since it is hardly conceivable that the tonsils or adenoids contribute essentially to hematopoiesis, at least after the first year or so of life, this idea will not be discussed.

The proponents of the immunity concept suggest that the lymphoid elements comprising Waldeyer's ring tend to confine upper respiratory infection and perhaps confer immunity.²⁹

Bloomfield has pointed out the adequate natural protective functions of the nose, mouth, pharynx and lungs. The logic of his statements, in the author's opinion, fully refutes the advocates of the tonsil immunity theory. Bloomfield⁶ wrote that the natural

• *It is doubtful that the tonsils or adenoids contribute sufficiently to immunity or to hematopoiesis to warrant withholding adenotonsillectomy when there is need for the operation. Focal infection, rheumatic fever and allergic disease must be evaluated in the individual case. A seldom discussed reason for operation is the prophylaxis or treatment of malformation of the nose, sinuses, mouth and jaw. Well defined indications for adenotonsillectomy include frequent occurrence of infection, peritonsillar abscess, cervical lymph node disease believed caused by tonsillar infection, otitis media, and hypertrophy sufficient to embarrass swallowing or breathing. The operation may also be indicated in certain cases of impaired hearing, halitosis, or anorexia, and sometimes for carriers of diphtheria.*

Psychic trauma can be obviated by proper preparation of a child for the operation he is to undergo.

There is a good deal of evidence of relationship between recent adenotonsillectomy and infection with poliomyelitis—and a good deal of evidence to the contrary. Nationwide rules cannot be established on the basis of the evidence presented thus far. Since in many cases it is unwise to put off adenotonsillectomy, each case in each community in each season must be evaluated separately.

design and function of the nose and pharynx is to prevent the lodgement of any foreign material or bacteria. By chance if bacteria were arrested in the tonsillar crypts, for example, infection might follow. The organisms if promptly eliminated, on the other hand, would be rendered harmless. He emphasized that the ability of the membranes to expel bacteria is one of the most important body defense mechanisms.

The great frequency of upper respiratory infection is evidence that any possible immunity is short-lived. The role of Waldeyer's ring appears, on this score, to be a poor contribution to the body's defense mechanism. Although it is questionable that the frequency of upper respiratory infection is diminished following adenotonsillectomy, the severity of infec-

tion is certainly lessened. The discomfort of a cold or sore throat is less after adenotonsillectomy, for the patient can breathe and can swallow more easily. When the tonsils and adenoids are a continuing source of infection, removing them must improve what is vaguely and commonly called "resistance." Quinsy, or peritonsillar abscess, is forever prevented.

Many children begin to blossom soon after adenotonsillectomy even though there was no indication before operation that infection was responsible for their failure to gain weight. Ashley² found a far greater gain of weight in 602 children who had had tonsillectomy than in 922 who had not.

Controversy over the relationship of the tonsils and adenoids to respiratory infection and to focal infection has continued over a long span of years. In perusal of 16 articles taken at random from the voluminous literature on the subject, it was noted that eight authors were in favor of tonsillectomy, three were in doubt, and five were opposed to the operation in consideration only of benefit in prevention or treatment of various types of infection.

Lower respiratory tract infection may be more frequent in persons who have had tonsillectomy, although statistics are difficult to obtain. Kaiser²⁶ followed the development of 4,400 children, half of whom had had the operation, for a period of ten years to adolescence. He felt that the removal of tonsils and adenoids lessened infection of the upper respiratory tract but that the effect with regard to lower respiratory infections was adverse. Kaiser found less middle ear infection in the children who had been operated upon but as much acute sinusitis, laryngitis, and nasal allergic disease in one group as in the other.

In another study, Kaiser²⁵ surveyed 48,000 school children, 20,000 of whom had undergone tonsillectomy an average of five years previously. Twelve hundred children who had signs of rheumatic fever, chorea, or heart disease were examined. Kaiser concluded that "the tonsillectomized child is assured greater protection against these infections than his companion whose tonsils have not been removed."

In a review of the indications for tonsillectomy and adenoidectomy, McFarland³¹ concluded that the effect of removal is beneficial in 80 per cent of cases.

Ashley⁴ found that time lost from school was the same for children who had had tonsillectomy as for those who had not. The weight gain was greater in those who had had the operation.

A great deal of the literature was reviewed by Cunningham.¹² She reported on a survey of 12,530 young white women who entered the University of California between 1920 and 1929. One-third had undergone tonsillectomy, one-third were thought to have pathologic abnormality of the tonsils, and one-third had normal tonsils. The results of the survey

made Cunningham question the value of the operation in the prophylaxis of infectious diseases and in the prevention or cure of such diseases as rheumatism, chorea, or carditis.

Boots and McCollom⁷ expressed belief that tonsillectomy may be of value in selected cases of rheumatoid arthritis, but not in certain other forms of arthritis.

A two-year postoperative study of 540 children by Epstein²⁹ convinced him that there was no correlation between the preoperative symptoms and result of the operation. Large tonsils were usually observed to be infected when studied histologically, but hyperemia of the pillars was not found to be significant. Good results were obtained in prevention of disease of the throat and fair results with regard to nasal disease.

Emenheiser¹³ stated that tonsillectomy is of no value in the therapy of disease that might be the result of a focus of infection. Coates and Gordon,⁸ on the other hand, urged careful analysis of each case to find those in which tonsillectomy might remove the source of infection. When chronic infection threatens to do more harm than the danger of operation, tonsillectomy is necessary, according to Shambaugh.³⁹

Allergic states have come to be recognized as commonplace within the last score of years. Although advances have been made in the therapy of such conditions, treatment is far from satisfactory. The relation of the tonsils and adenoids to allergic disease is a subject of controversy. Twelve investigators whose reports were consulted were evenly divided in opinion. Six stated that adenotonsillectomy was contraindicated in children with allergic disease. The other six expressed the belief that the indications for the operation are the same in allergic as in nonallergic children, but some of them advocated treatment of the allergic condition before operation.

A point apparently overlooked is that children with allergic disease affecting respiration need as open an airway as possible. If an adenoid mass is large enough to contribute to obstruction, removal is necessary; and the tonsils should be removed at the same time to obviate need for a secondary procedure. At the same time the nasal passages may be dilated by means of passing a firm endotracheal-type tube through the nares into the nasopharynx. The dilation not only compresses the turbinates with a minimum of trauma but produces a degree of tissue shock that in itself gives some measure of relief.

Apart from considerations relative to the factors of hematopoiesis, immunity and allergic disease, about which there is so wide a diversity of opinion, there are well defined causes for adenotonsillectomy. Among these are otitis media, occurrence of repeated moderate to severe infections even though there be no

peritonsillar abscess or enlargement of cervical lymph nodes, and hypertrophy sufficient to embarrass swallowing or breathing. It is difficult to decide, on the basis of size alone, whether operation should or should not be done. A small amount of adenoid tissue, for instance, may cause considerable pathologic change in the ears. In adults the matter of size is given more weight during examination, for usually the tonsils atrophy after the first or second decade of life unless stimulated by disease. Hyperemia of the pillars may be similarly difficult to judge. When the tonsils have undergone severe Vincent's infection or when they are a source of halitosis, removal is necessary. In some cases it has been possible to release carriers of diphtheria from quarantine after extirpation of the tonsils.

A less well known but equally important indication for adenoidectomy is the prevention or treatment of malformation of the nose, mouth, or jaws that has resulted from so-called adenoid facies. In persons who breathe through the mouth, the hard palate and upper dental arch may become narrowed owing to a lack of support by the mandible. The palate is not only narrowed so that there is not enough space for all the teeth, but elevated. The nasal space is thereby restricted and the growing nasal septum deflected, which further interferes with nasal breathing. Moreover, stimulus for growth of the mandible may be deficient and the orthodontic problem thereby compounded.

The rare but terrible catastrophe of malignant disease of the tonsil is obviated by tonsillectomy. The "five-year cure" rate for carcinoma of the tonsil is very low.

Definite contraindications to adenotonsillectomy include the presence of acute infection, blood dyscrasia, uncontrolled diabetes, and cardiac and renal disease until completely investigated. Proven cases of death from disturbance of the thymus by tonsillectomy are most rare, and it may be possible to prevent such occurrences by making preoperative studies of the response to cortisone or corticotropin (ACTH).

PSYCHIATRIC CONSIDERATIONS

The essence of the objections to tonsillectomy voiced by some psychiatrists^{5, 9} seems to be that the mental trauma of the operation, produced by the unusual and therefore frightening experience at an impressionable age, may be the foundation of a psychiatric problem that develops later. Responsibility for this situation is laid wholly at the door of surgeons who, not recognizing the possibility of psychic trauma, do not allay a child's anxiety by letting him know what to expect. In this psychiatric view, younger children should be heavily premedicated or

basally anesthetized as a means of prevention. Save for the recommendation regarding anesthesia, the foregoing is reasonable to otolaryngologists. (The dangers of basal anesthesia will be discussed later.) What has not been pointed out sufficiently is that tonsillectomy (or any other operation at an early age) is not the only hurdle a child must, of necessity, jump. Weaning, punishment by the parent, the initial visit to the barber shop, the first injury, and the first day of school also may be memorably unpleasant and could inflict mental scars. Usually they do not because the parent is ready to give guidance. Similarly, the parent, with the help of the physician, must prepare a child for an operation. Even younger children can be lightly premedicated and soothed. Tonsillectomy, then, need not cause lasting psychic trauma but can become rather another important stepping stone, an obstacle adequately understood and conquered, even useful in training a child's mind to meet the further problems needed for development. A surgeon's obligation lies not only in careful and adequate operation but also in the coaching of the parent and the child. Most surgeons of the author's acquaintance believe the time given to pre-operative education is time well spent.

THE POLIOMYELITIS PROBLEM

Although the possibility of a relationship between poliomyelitis and tonsillectomy was first suggested by Sheppard's⁴⁰ report of the 1910 epidemic in Springfield, Mass., little interest was aroused until 1928 when the study of Aycock and Luther³ was published. Controversy over the issue has not become widespread until about the last decade. The reports by Krill,²⁸ and others, of the K family disaster of Akron, Ohio, were undoubtedly a stimulus.

Even in communities where the winter climate is not severe, upper respiratory tract infections are most frequent at that time of year, which would seem to indicate the summer months as the most propitious time for adenotonsillectomy. Yet the procedure often is postponed, even in cases in which it is much needed, owing to an almost universal voluntary ban on elective operations about the head during times when poliomyelitis is epidemic. This despite the fact that it has been difficult to establish criteria for an epidemic of poliomyelitis in localities where there are cases of the disease at all times of the year, even winter.

There have been numerous attempts to clarify the problem by statistical and experimental means. In a review of the available literature it seemed that there was about equal division between three opinions: (1) that there is a definite relationship between the operation and poliomyelitis; (2) that it is doubt-

ful there is such relationship or, if there is, the risk is small; (3) that there is no relationship between the operation and the incidence of poliomyelitis. Most of the articles expressing the latter opinion were of fairly recent date. The studies by which the three opinions were arrived at were based on a greatly variable number of cases, and several encompassed a review of the literature.

Cunning,^{10, 11} for example, under the auspices of the American Laryngological, Rhinological and Otological Society, gathered data on 36,678 cases of poliomyelitis and 96,379 tonsillectomies. Of 35,039 patients who had had tonsillectomy during the years 1937 to 1949 and were followed for a two-month period postoperatively, only five contracted bulbar poliomyelitis. Faber¹⁷ criticized the statistical method used by Cunning and reported a different incidence using part of the same data.

Even in evaluation of seasonal and epidemic factors, agreement cannot be reached. Siegel,³⁸ and others, found that the evidence in support of a tonsillectomy-poliomyelitis relationship was stronger in non-epidemic years, and in the spring and fall. They were of the opinion, however, that winter was the safest period for the operation, considering only poliomyelitis. In the severe epidemic of southwestern Iowa in 1948-1949, Treynor⁴² discovered no connection between poliomyelitis and tonsillectomy. In Los Angeles County, Miller³² carefully compiled statistics on 1,229 cases of poliomyelitis in the severe epidemic of 1949. He found no reason to discontinue tonsillectomy in the summer months.

On the other hand, Goerke and Bower,²⁰ reporting on data on poliomyelitis in California from January 1948 to March 1949, in addition to some other cases presented in the same article, gave statistics implicating tonsillectomy in relation to bulbar poliomyelitis. Neither Stebbins⁴¹ nor Seydell^{36, 37} who studied severe summer epidemics during which time tonsillectomies were done could conclude definitely either that there was or was not relationship. McCormick³⁰ discovered a much higher incidence of poliomyelitis in persons whose diet was supplied by charity.

From statistics available, therefore, it cannot be said definitely that a relationship exists between poliomyelitis and tonsillectomy. One case of bulbar type poliomyelitis following tonsillectomy is sufficient cause for a pause for reflection, but stronger evidence is needed to prove a cause-and-effect relationship.

Ingalls and Aycock²⁴ reported upon a severe epidemic of poliomyelitis in a boys' school resembling in every way the epidemics in which tonsillectomy has been indicted. In that epidemic, however, adenotonsillectomy was not a factor and upper respiratory tract infection was thought to be a factor in susceptibility.

The solution to the problem may be found when it is discovered why clinical poliomyelitis, especially that of bulbar type, develops in the absence of any so-called inciting incidents such as tonsillectomy, dental extraction or inoculation. The very fact that so many things, some non-surgical, are suspected suggests an unknown factor. It would be worth while of course to prevent even one case, but does postponing inoculation or operation prevent any? And if risk there be, is it great enough to warrant postponing such procedures if there is great need for them? Why is poliomyelitis in many cases so mild that it is not clinically recognized? Experiments conducted by Sabin,^{33, 34} Faber,¹⁵⁻¹⁹ Schultz, Bodian and Howe,^{22, 23} von Magnus and Melnick,⁴² and their associates, have failed to answer these questions.

In cynomolgus monkeys clinical poliomyelitis can be readily produced by nasal instillation of the virus. With the nasal pathways blocked, the disease is not so easily induced through the intact mucosa of the mouth or pharynx. When the virus is injected into tonsillar or peritonsillar tissue of the monkeys, or fed to them soon after tonsillectomy, nearly all develop clinical poliomyelitis. If the virus is introduced into the pharynx and tonsillectomy done soon afterward, bulbar paralysis takes place. Clinical manifestations can be prevented, however, by swabbing the animal's throat with iodine a few minutes before the operation is performed.¹⁹

The virus has not been observed in tissues other than those of the nervous system, the tonsils, or the alimentary tract. The upper portion of the gastrointestinal tract is more vulnerable than the lower. The virus has been recovered from the stools and from the tonsils of patients with active cases and of asymptomatic carriers during epidemic periods many times. It has also been recovered from feces and from tonsils in interepidemic periods.²⁷ Immunity conferred by infection with one of the three types of poliomyelitis virus does not protect against the others.

The use of gamma globulin,^{4, 21} potassium and local antisepsis¹⁹ offer some promise in prophylaxis. In vitro, gamma globulin is capable of neutralizing all three kinds of poliomyelitis virus, provided the pooled human plasma from which it is prepared comes from a wide enough range of sources.

THE OPERATION

Basal anesthesia for children undergoing adenotonsillectomy has been revived by the use of sodium pentothal rectally^{1, 44, 45} in response to the warning against psychic shock. To the author, light premedication, induction with Vinethene® (divinyl ether) and then use of ether for anesthesia seems safer. Quick arousal lessens the danger of pulmonary com-

plications. It is not necessary to give heavy preliminary sedation to avoid psychic shock.

Although at the time of operation the indication may be much less for one than the other, usually adenoid tissue and the tonsils are removed at the same time in order to avoid possible necessity for another operation later. Modern anesthesia, asepsis, illumination and hemostasis have rendered mortality rates very low. These same advantages, however, making it possible for insufficiently trained surgeons to carry out the operation, may be a factor in the too high morbidity rate. The avoidance of complications demands exacting technique, familiarity with head illumination, and aptitude in securing hemostasis in a field not easily accessible.

Scarring of the palate, the leaving of tonsillar remnants, and removal of the pillars or uvula are undesirable but not noted readily by the patient. Poor results cannot be explained away, however, as inherent in the nature of the operation, or by implication that the tonsils "grew back." The nonencapsulated adenoid tissue may again hypertrophy, but at the time of operation, direct inspection of the nasopharynx by gentle retraction of the palate permits clean removal and the torus of each eustachian tube remains undisturbed.

Subsequent hypertrophy or hyperplasia of other components of Waldeyer's ring may be prevented by assiduous adenoidectomy and attention to the entire area at the time of operation. It is not necessary to be radical in order to be thorough. Radical procedures produce excessive scarring in this region. In a few cases, x-ray therapy may be required for shrinkage of tissue.

Following a properly performed adenotonsillectomy, there is minimal scarring, and the pillars, palate, and uvula remain intact. Painstaking, yet not overly long, sharp and blunt dissection, followed by snaring, is the method of choice. All of the tonsillar and adenoid tissue, but nothing else, should be removed. Should operative or postoperative hemorrhage occur, the surgeon alone should be able to control it immediately and completely.

With the new advances, the operation may be of benefit to younger patients, preferably three or four years of age. Severe infection, impaired hearing and malformations of the nose and mouth may be prevented. Age is not a contraindication in a child with impaired hearing caused by adenoid obstruction.³⁵ If such hearing defects are not adequately relieved by surgical treatment, excellent results usually are obtained by irradiation. In uncooperative children, x-ray therapy may do better for this purpose than the radium applicator, which must be precisely placed and maintained in place for many minutes.

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Anesthesia in Cardiac Operations

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ALMOST WITHOUT exception every drug administered in the production of anesthesia is a depressant of physiological functions, not only of the central nervous system but also of the cardiovascular system. How much poisoning can a patient tolerate and still survive? This is the primary problem faced by the anesthesiologist in the management of patients who are being operated upon. For successful solution of the problem, particularly as it is presented in connection with cardiac operations, it is essential that each member of the medical team involved—cardiologist, surgeon and anesthesiologist—have all knowledge possible about the status of the disease and the physiological reserve of the patient. Then, should emergency arise, valuable time need not be lost in discussion.

To accomplish the desired teamwork in the management of patients undergoing cardiac operations, the following approach has been developed at the Los Angeles County Hospital. First, the patient receives a complete diagnostic study in the cardiology department, including cardiac catheterization where indicated. The patient then is presented to a conference attended by the cardiologists, surgeons and anesthesiologists responsible for his care. At this conference the following decisions are made: (1) whether or not the patient is a suitable candidate for operation; if so, (2) which operation offers the best chance of improvement, and (3) when operation should be undertaken.

If the patient is a suitable candidate and is in optimal condition, the operation is scheduled for a definite date. The patient is then admitted to the hospital at least three days before operation to give time for final evaluation of his condition and for immediate preoperative preparation. Each member of the team examines the patient again during this preoperative period.

In the ten months following establishment of this regimen, 33 patients were operated upon, including 20 in whom mitral commissurotomy was done and

• *When the team of physicians—cardiologist, anesthesiologist and surgeon—who are to attend a patient during a cardiac operation study the patient together in preoperative evaluation, they are better able to anticipate emergencies that might arise during the procedure and to deal with them without loss of time for discussion.*

The principal problems of the anesthesiologist during operation are maintenance of adequate ventilation and oxygenation, maintenance of the lightest level of anesthesia possible (the minimum degree of poisoning), and maintenance of adequate circulation. The cardiologist must maintain constant observation of the heart rate and rhythm and be alert for early signs of myocardial oxygen deficiency.

there were no deaths during operation; there was only one fatality in the postoperative period (caused by cerebral thrombosis in a patient with tetralogy of Fallot), and there has been only one patient whose condition deteriorated so much during operation that the procedure had to be abandoned. The latter patient made uneventful recovery and will be operated upon again.

The formulation of the philosophy of management of these patients was based on the knowledge that each of the anesthetic and protective drugs that may be used is a depressant. Therefore, the number of drugs used and the dosage of each has been reduced to the minimum consistent with the successful completion of the operation. No drugs are used prophylactically. Procaine amide and quinidine are not administered preoperatively. A continuous procaine infusion is not used during anesthesia and operation. Procaine is not applied topically on the myocardium. The left auricular wall is not infiltrated with procaine prior to the placing of sutures. If, during operation, the use of these or other drugs is indicated, then and only then are they used. Drugs such as digitalis, which the patient may have been receiving on a maintenance basis, are continued as usual. By strictly limiting the number of drugs active in the patient at the time of operation a much more accurate evaluation of the cause or causes of any change in the patient's condition may be made. With

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this approach, rational therapy can be instituted as indicated when the need arises. Minute to minute information regarding the function of the patient's heart is obtained by continuous observation of a direct-writing electrocardiogram by the cardiologist member of the team. The function of the cardiologist is of utmost importance in the care of these patients during anesthesia and operation, for he can detect changes long before they become evident clinically, and appropriate therapy or corrective measures can be instituted earlier.

ANESTHETIC MANAGEMENT

The desired result of pre-anesthetic medication is tranquillity for the patient without depression of physiological compensatory mechanisms. This can be achieved in patients undergoing mitral commissurotomy, for example, with small doses of Demerol® (25 to 50 mg.) and scopolamine (0.3 mg.). However, it should be emphasized that the dosage is individualized for each patient. Scopolamine is used in preference to atropine for three reasons: (1) sedative and amnestic properties, (2) better drying of pharyngeal and tracheobronchial secretions, and (3) less pronounced vagal blockage. Demerol is used because, in comparable doses, it does not depress the circulatory and respiratory systems as much as morphine. Patients are not given barbiturates by mouth because these drugs may cause circulatory depression and the effects are unpredictable.

A smooth induction is mandatory for a patient who is to have a cardiac operation, since an excitement stage is equivalent to violent exercise. Quiet induction can be accomplished with 50 to 200 mg. of pentothal intravenously or with cyclopropane and oxygen. The patient is then anesthetized deeply enough with cyclopropane so that there is no "bucking" or reaction when an endotracheal airway is inserted. Inflation of a rubber cuff attached to the endotracheal airway provides an airtight tracheal seal.

From this point on, anesthesia is maintained with cyclopropane and oxygen or ether and oxygen. The authors wish to emphasize, however, their conviction that cyclopropane should be utilized in the management of these patients only by anesthesiologists who have had extensive experience with the use of this agent. Anesthesia should be as light as possible, consistent with smooth maintenance and the requirements of the operation. Remarkably small amounts of anesthetic agents are needed. For example, ordinarily only 10 to 30 cc. of ether is required for a two-hour mitral commissurotomy.

During the maintenance period the most important problems are:

1. Maintenance of adequate respiratory exchange in the presence of an open pneumothorax in a patient with a low respiratory reserve, whose position further embarrasses the function of the unopened side.

2. Maintenance of adequate circulation in patients with very low cardiac reserve, and the prevention of shock.

3. Control of arrhythmia, including tachycardia.

The first of these problems, adequate ventilation, is the direct responsibility of the anesthesiologist. A perfectly clear airway is a primary requisite. The effect of oxygen want on the myocardium becomes evident early. Reduction in oxygen supply is a most serious hazard and leads not only to malfunction of the myocardium but also to arrhythmia, which in turn decreases cardiac output. This leads to inadequate flow of blood through the coronary arteries and, in a vicious cycle, to the production of more myocardial ischemia. Adequate ventilation can be achieved by assisted respiration or controlled respiration according to the given need from moment to moment. Controlled respiration produces a quiet operation field which is especially important during anastomosis of blood vessels. It should be emphasized that the method of providing adequate ventilation is not particularly important so long as an adequate exchange of oxygen and carbon dioxide occurs.

Circulation should be maintained by adequate blood replacement as blood is lost. Keeping two intravenous portals open by a slow infusion is advisable so that, if needed, they are immediately available at all times for blood or drug therapy. Thus far since the inauguration of the previously outlined regimen for patients undergoing cardiac operations, need for use of vasopressors has not arisen, and such drugs are not used prophylactically. As would be expected, arterial blood pressure frequently becomes undetectable during the manipulation of the mitral valve, owing to mechanical obstruction of the flow of blood within the heart. This period is brief (a matter of seconds) and no therapy is required. Occasionally severe arrhythmia, precipitated by manipulation of the heart or pericardium, causes a fall in systolic blood pressure. Recovery is prompt following cessation or modification of the manipulation. In event of massive hemorrhage, an ever-present hazard, intra-arterial transfusion is certainly the method of choice for replacement. Shock did not occur in any of the 33 cases in the present series, owing to maintenance of the lightest possible anesthesia and replacement of blood loss at the time the loss occurred.

In order that arrhythmia may be noted immediately if it occurs, a continuously recording electro-

cardiogram is connected before induction of anesthesia and the tracing is observed continuously throughout the operation by the cardiologist, who immediately reports any significant change to the other members of the team. When change in rhythm occurs, the operation is temporarily halted, if necessary, until the cause has been ascertained and corrected. For example, if pressure on the heart by a rib-spreading retractor causes ventricular extrasystoles, the position of the retractor can be changed. In the present series arrhythmia that occurred from other than mechanical causes was controlled by *improving the ventilation* and inflating the collapsed lung while resting the patient. On only two occasions was the administration of procaine amide necessary for the control of persistent ventricular arrhythmia. In the authors' experience the incidence and severity of cardiac arrhythmia is no greater with cyclopropane than with ether.

Brief rest periods are given the patient periodically, especially just before the definitive part of

the operation. During these periods all operation ceases and the collapsed lung is inflated and kept inflated until the rest period is over.

Every effort is made to have the patient fully conscious at the end of the operation. The tracheobronchial tree is cleared before the endotracheal airway is removed. The systolic blood pressure should be within 10 to 20 mm. (mercury) of the pressure that is normal for the patient and the pulse rate should not be over 120 beats per minute. Respiration should not be depressed to any degree.

Postoperatively, the patient is followed closely by each member of the team. If complications develop, appropriate therapy as decided in consultation by the members of the team is carried out. The only serious postoperative complication in the present series was one of respiratory obstruction from tracheobronchial secretions compounded by an overdose of an analgesic drug. An emergency tracheotomy was necessary for removal of the secretions and the patient made uneventful recovery.

Transorbital Lobotomy

Its Use in Relapsing Psychotic States

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IN PRIVATE PSYCHIATRIC practice the authors have recommended the conventional radical prefrontal lobotomy only in cases of very refractory chronic mental illnesses. In a previous report¹ attention was called to some of the drawbacks, especially the prolonged period of rehabilitation. The use of so radical a procedure in affective disorders or psychoneuroses was questioned, and the opinion was expressed that the main use for the procedure was in the treatment of chronic schizophrenia.

Since the advent of the simplified technique of transorbital lobotomy and with it an increasing number of satisfactory clinical results with few complications, the authors have recommended the procedure in a variety of conditions and at a much earlier period in the patient's mental illness, as a preventive of permanent chronic mental illness.

The present communication concerns 25 cases in which transorbital lobotomy was performed on private patients from a general hospital psychiatric department. The experience differed somewhat from other reports of more chronic cases from state hospitals. However, all of the patients were so disabled and refractory to other kinds of therapy that commitment to a state hospital was imminent. Lobotomy was advised when there was poor prognosis for relief by further treatment of conventional type.

Freeman^{2,3} described the indications, technique and complications of transorbital lobotomy, emphasized the benefit in early schizophrenia, and recommended the treatment in cases of involutional depression that are resistant to electroshock or in which maintenance therapy is necessary. He pointed out that with the less extensive transorbital lobotomy there are fewer undesirable effects than with the standard procedure. In transorbital lobotomy areas 9 and 10 are undercut and only about a third as many frontothalamic fibers are sectioned as in the standard procedure. Hence there is better preservation of personality.

Well over 100 transorbital lobotomies were reported from 1946 to 1948. Jones and Shanklin⁴ reported that of 41 patients operated on in a state

• Twenty-five private patients were treated by transorbital lobotomy. The period of observation after operation was from six months to three years. In 14 cases of affective disorders in which there was not adequate response to shock therapy, nine patients made social recovery and maintained good health and four were improved. Some follow-up shock therapy was necessary for about one-fifth of the patients. Of eight schizophrenic patients four made excellent social recoveries, two improved and two were not improved. In three cases of obsessive compulsive states, results were not satisfactory.

In light of the factors of less disturbance to the total personality, absence of postoperative complications, shortened hospitalization, pecuniary savings and better clinical results, the authors prefer transorbital lobotomy to prefrontal lobotomy in private psychiatric practice and believe that in cases of frequent relapse early use of the procedure should be considered to prevent development of a chronic state.

hospital service, 16 were improved enough to warrant parole and 12 showed fair results but remained in the hospital. In a later report on 92 cases⁵ these investigators pointed out the great advantage of the procedure in selected cases of chronic involutional depression. More recently Moore, Hill and Lutz⁶ reported upon use of the operation in 102 patients, most of them schizophrenic, in a state hospital. Over-all improvement was noted in 88.2 per cent of patients and recovery in 29.4 per cent, all of whom had disease of paranoid and catatonic type. Stevenson and McCausland⁷ recommended prefrontal leukotomy to prevent recurring manic-depressive illness, for patients who relapse with electroshock or who cannot be carried on maintenance treatment. In a small series followed four years there were no recurrences.

Of the 25 patients in the present series, 14 had been observed for one to three years at the time of this report, and 11 for one year or less. Two were men, 23 women. The age range was 20 to 82 years.

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Two were past 60 and four were between 20 and 30 years of age. Diagnoses were as follows: Affective disorders, 14; schizophrenia, 8; obsessive compulsive neuroses, 3.

All of the patients had previously been treated by shock. Those with affective disorders had had repeated courses of electroshock in an average of four periods of hospitalization, but remission was not enduring. The schizophrenic patients had been given both electroshock and insulin shock treatment without lasting benefit and the average number of admittances to hospital in this group was five. The patients with obsessive compulsive psychoneuroses had been given psychotherapy, electroshock and subshock insulin treatments without success.

SURGICAL PROCEDURE

The transorbital technique used on these patient followed that described by Freeman.² In one case, that of a patient with advanced paranoid schizophrenia with auditory hallucinations, no improvement followed transorbital lobotomy, and radical lobotomy then was carried out, also without benefit.

Complications: One of the patients died of frontal lobe hemorrhage. At necropsy malignant growth, metastatic from a cancer of the breast for which mastectomy had been done previously, was noted. Third nerve palsy that lasted a few days occurred in another case. All other patients made uneventful prompt recovery from the operation and were well enough to leave the hospital in from two to four days after it was done.

Results: Results in the 25 cases are listed in Table 1.

The best results occurred in patients with affective disorders; nine of the 14 patients in the group were rated socially recovered and four as improved although two of them required further maintenance of electroshock therapy. In the schizophrenic group the best results were obtained in patients with the catatonic variety of the disease with affective admixtures of excitement or depression. The three patients with catatonic schizophrenia who were considered "socially recovered" required further postoperative electroshock therapy. One patient with chronic paranoid schizophrenia had no sustained improvement and no abatement of hallucination after orbital lobotomy or, later, after radical lobotomy.

The following reports are illustrative of the results obtained in cases of various types.

CASE 1: Affective disorder, agitated depression.

The patient, a woman 50 years of age, was admitted to the Herrick Memorial Hospital for the first time on December 18, 1949. A nurse for many years, she had never married and was living with two widowed sisters. The first onset of depression was in 1948, when the main content of the patient's thoughts centered around her "unforgivable sins"

TABLE 1.—Results of Transorbital Lobotomy in 25 Cases

Diagnosis	No. Patients	Result*		
		A	B	C
AFFECTIVE DISORDERS				
Manic-depressive	5	4	1	
Agitated depression	2	2		
Presenile depression	3	1	2	
Involuntional melancholia	4†	2	1	
SCHIZOPHRENIC				
Catatonic	4	3		1
Paranoid	2		1	1
Mixed (schizoaffective)	3	1	1	1
OBSESSIVE COMPULSIVE				
Total	26	13	8	4

*A—socially recovered—that is, with good adjustment at work or at home, without evidence of psychotic symptoms; B—improved and able to be with their families, but with residual manifestation of psychotic illness; C—unimproved, requiring institutional care.

†One died.

and the feeling that she was no good. All her preoccupations were directed to decreasing her self-esteem. A series of 14 electroshock treatments brought some improvement but the obsessive ideas continued. In February 1950 she again became depressed, agitated and self-deprecating. At her second admittance, February 25, 1950, she had lost 40 pounds in weight. The patient was given 32 electroshock treatments and then maintenance electroshock every two weeks. Improvement was slight and relapses frequent. Transorbital lobotomy was performed August 5, 1950. Immediately pronounced mental and physical improvement occurred. After remaining at home the rest of the year the patient resumed nursing. At the time of report she had remained entirely well for 18 months.

CASE 2: Schizoaffective catatonic, depressive and paranoid features.

The patient, a woman 26 years of age, was admitted to hospital on January 22, 1951. Three days after the birth of her first baby (Jan. 11, 1951) she had returned to a home situation in which no outside help had been planned except for that of her mother-in-law. The baby would not nurse and cried almost constantly. The mother-in-law became very upset and the husband wished to take no responsibility. The patient wept and could not sleep because of worry about the baby. To her own mother, who was then summoned, she could talk only about her hospital experiences, her dislike of the doctor "who let her suffer" during the birth, her fears of the spinal puncture and the episiotomy. She worried about taking narcotics and becoming an addict. She felt that her baby was abnormal, that she was losing her mind, and that her body and mind were disconnected. She talked about the motion picture "Snake Pit" and begged her mother not to send her to such an institution.

The family physician referred her to a psychiatrist. In spite of her strong resistance, shock treatment was started in the office. Once when the patient was left in the room by herself, she slashed her wrists with a razor. She was then hospitalized.

On admittance the patient appeared tense, suspicious and very depressed, with much blocking. At times she was withdrawn, mute and catatonic; at other times she would become actively hostile, necessitating seclusion. She made several suicidal attempts. A series of 24 electroshock treatments was given, without sustained improvement, followed by 13 insulin coma shocks. Transorbital lobotomy was performed May 21, 1951. The change in the patient's behavior and attitude was immediate and dramatic. All paranoid features disappeared; mild anxiety remained for a time

and the patient felt insecure at home for a short period. At the time of report she was receiving electroshock treatment at monthly intervals and was carrying on all home responsibilities without difficulty. Her recovery was considered to be extremely good.

CASE 3: Schizophrenia, paranoid type.

A 60-year-old woman was admitted to hospital on October 20, 1950. In 1940 the patient had begun to worry about the menopause. Once she spoke about her nephew, who was involved in wartime maneuvers, and thought perhaps the government was after her because she had given out restricted information. Shortly thereafter she was unable to eat. Later the depression disappeared but she would talk to herself. In 1946 she began to imagine that people whom she had known from childhood were trying to do such things to her as spoiling her looks. She would shout aloud, and the neighbors complained that she shouted all the time her husband was away. She felt that the neighbors were against her. Nine electroshock treatments were given and there was slight improvement. The patient then refused further psychiatric treatment. Soon she again heard voices that she would answer in loud tones, and she became progressively worse. Transorbital lobotomy was performed October 23, 1950. The patient did not improve and the auditory hallucinations continued. On October 31, 1950, radical prefrontal lobotomy was performed, also without improvement. The patient was committed to a state hospital some months later.

CASE 4: Obsessive compulsive neurosis, schizophrenic features.

A man 20 years of age was admitted April 27, 1950. Compulsive habits had begun at age 14 when he repeatedly marked articles in his wardrobe and said that he suspected thefts. At age 16 he became extremely fussy about his haircuts and the style of combing his hair. Later he started pounding the steps with his foot several times before going up or down stairs, and he would also compulsively repeat such acts as going up or down stairs or closing the gate. He lost interest in his studies except for music. By Christmas of 1949 he was much worse, and would remain in bed until late in the afternoon listening to the radio. After getting up he would spend two hours or more in breathing exercises like blowing a paper against the wall and would use another two or three hours in the bathroom, washing himself and dousing his eyes with cold water. He would repeatedly manipulate his penis with a towel, paying no attention to his mother's observation. In February 1950 he had several interviews in a mental clinic but did not cooperate. In April he was admitted to Herrick Memorial Hospital, where transorbital lobotomy was performed on May 17, 1950. The patient showed fair improvement for a time, but gradually reverted to the old obsessive compulsive pattern. He was unable to make adequate social adjustment outside the home.

INDICATIONS FOR TRANSORBITAL LOBOTOMY

The authors consider the results obtained with this modified, less traumatic lobotomy procedure at least equal to and perhaps better than those obtained by the radical operation, and recommend its use relatively early in selected cases in which it appears mental disease may become chronic.

In affective states in which a reasonably adequate course of shock therapy has failed to bring sustained recovery or in which there is early or frequent relapse or lack of response to maintenance shock ther-

apy, transorbital lobotomy has given uniformly good results. In about a fifth of schizoaffective cases, some postoperative electroshock treatment has been necessary. However, fewer treatments are needed in order to hold the patient in good emotional control, and the treatments are more easily administered. Transorbital lobotomy also is recommended for schizophrenic patients who have not responded well to both insulin and electroshock and in whom either distinct affective components or aggressive paranoid symptoms are present. The authors agree with Stevenson and McCausland that prophylactic leukotomy offers the best hope for breaking the recurrent cycles of manic-depressive illness.

Pecuniary factors and emotional considerations in the family of the patient enter into decision between lobotomy and prolonged hospitalization and shock therapy. When the outlook is that of prolonged expense for treatment or of a decision for commitment to a state hospital, the authors discuss with the relatives the advisability of lobotomy. From the standpoint of private practice, transorbital lobotomy has considerable advantage over the more radical prefrontal operation. The radical procedure entails a long period of postoperative somnolence and apathy, and rehabilitation and nursing management are costly. Complications such as prolonged incontinence and organic epilepsy are not infrequent, and bulimia caused by posteriorly placed incisions occasionally occurs.

None of these problems occur in connection with transorbital incisions. There is less of the frontal lobe syndrome following transorbital operation. The less extensive operation brings about sufficient change, such as loss of self-consciousness and of anxiety and lessening of hostility, to produce the desired clinical results without the more pronounced tactlessness, lack of concern and indifference that follow the radical procedure.

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The Role of Psychotherapy in Allergy

Credits and Debits

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IN RECENT YEARS allergists, like all other specialists and general practitioners, have studied the relationship of psychotherapy to their specialty. Newspaper and magazine publicity on psychotherapy and its relation to allergic conditions has led to confusion in the minds of the public. Especially confused are patients with allergic disease who are being treated according to accepted procedures.

Dunbar's² review of the literature on psychosomatic interrelationships in bronchial asthma begins with the comment that it is a controversial subject. Certainly all allergists must agree on that point.

F. Reichmann in 1922 concluded that bronchial asthma is a neurosis of the respiratory tract, a part manifestation of a general psychopathic constitution. She stated that not the "what" but the "how" is the decisive factor in the treatment of asthmatic persons. Marcinowski in 1913 wrote that asthma is due to a "basic anxiety hysteria." Numerous other investigators call asthma a reflex neurosis, or secretory neurosis, or a central or bulbar neurosis.

E. Marx in 1923 disagreed with the conception that asthma is psychogenic. His conception was that, in predisposed persons, organic disease stimulates "spasm centers" and that, later, psychic stimuli may increase the tension in these centers to a sufficient degree for the tension to be discharged as spasms of the bronchial musculature.

E. Moos in 1923 wrote that the psyche is almost always the primary, most usual and most important factor in the production of asthma. He later (1928) used intensive psychotherapy on a number of patients and came to the conclusion that although allergenic substances may represent an increased stimulus for an attack, the psychic attitude can prevent, inhibit or favor an attack.

K. Hansen in 1930 wrote numerous articles on the subject. He concluded one of his papers as follows:

"1. I am inclined to refute the interpretation of asthma, the disease as well as the single attack, as a psychogenic effect in the sense of a primary immediate expression.

"2. The disease and at least the first attack are in every case anatomically and physiologically, i.e., or-

• *Psychological problems play an important role in the production and exacerbation of allergic disease, just as they do in other illnesses, especially those of a chronic nature entailing economic and social problems. Some psychotherapy is implicit in the practice of all physicians. While most patients make satisfactory progress with whatever treatment is outlined, a few do not, and they may be helped if a little extra time is taken to investigate and rebalance their mental environment. In the treatment of patients with allergic disease, dealing with emotional problems is considered as adjunctive to specific desensitization.*

ganically, determined, and not a form of psychogenic reaction.

"3. The single attacks may be precipitated, furthered or inhibited by psychic factors."

J. Naber (1929) wrote that he was of the opinion the precipitating factor in every attack is a psychic one, and on this basis all his patients were cured by psychotherapy without medication, change of climate, etc. He stated that a person may have asthma without a neurotic component, or it may be psychic without a somatic component. Most cases are doubly determined—that is, in a person with allergic predisposition, the psychic factors mobilize the latent factors of the disease and make it apparent.

Wittkower and Petow (1931-32) reviewed the literature and stated that the importance of the psyche in the precipitation of asthmatic attacks has been known for a long time. They continued that frequent conditioning of attacks by situation is often compatible with and explainable by allergic factors. Other aspects—for example, the precise fixing of the time of the attacks—cannot be explained in many asthmatic persons without resorting to the considerations of psychic mechanism.

Bierman and Stokes¹ reviewed approximately 80 articles in German, English and American literature on eczema, asthma, and hay fever. Most of the articles cited one or two cases as conclusive that the psyche is the most important consideration and that psychotherapy is the treatment of choice. In their review,

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which was essentially a plea for tolerance, cases were cited which seem ridiculous to the author of the present communication. Gilespie cited a case of fungous infection of the hands which cleared only after the adjustment of an unsatisfactory parental relationship. In another case, reported by Pearson, a patient with sweaty feet and dermatophytosis was cured by psychotherapy when he was relieved of fear of his parents.

Rogerson and Hardcastle⁶ reported upon a study of 25 children with allergic disease and concluded that nervousness was a prominent symptom. Personality difficulties and environmental stresses played an important role in the condition, in that all the children were "overprotected" by their parents. This "overprotection" resulted because the children, for some reason, were especially valued by the parents, or because the children were fundamentally unwanted. The authors stated that although the reasons seem opposed, the fault lies in the personality of the parents, whose insecurity and overanxiousness are reflected in the nervous child.

McDermott and Cobb⁴ made a study of 50 patients in the allergy clinic and medical wards of the Massachusetts General Hospital. They found that in 30 cases there was a strong emotional factor, in seven some emotional disturbance, and in 13 none. In 20 patients emotional stimulus was the precipitating factor in the first attack—very definitely so in ten cases. Emotional stimulus precipitated later attacks in 21 patients. These investigators expressed belief that if the emotion, such as hate or eroticism, is of sufficient intensity the patient secretes enough epinephrine to stop the asthma. (The author has never seen an attack of asthma terminated by intense emotion.)

In 1941 a *Psychosomatic Medicine* monograph was devoted to psychic factors in bronchial asthma. The work was done at the Chicago Institute for Psychoanalysis by French and Alexander with the collaboration of Dr. Ben Rappaport and 11 psychiatrists. Twenty-seven patients were studied, 16 adults and 11 children who were selected because of having both emotional conflicts and asthma. The findings therefore cannot be conclusive as to frequency and relative importance of emotional factors as compared to allergic factors. Patients were studied for from two weeks to 43 months.

The authors frankly admitted the speculative nature of their conclusions, which they summarized as follows:

1. The separation from the mother is the central emotional problem.
2. Asthma is related to the suppressed cry for the mother.

3. The mothers of asthmatic persons are often of the rejecting type.

4. Some mothers of asthmatic persons show pronounced pride in the early independence of the child.

5. Breathing of the newborn represents the first step toward a biological independence of the child from the mother.

6. Asthma often appears in early childhood.

7. The sexual impulse seems to be most significant in precipitating attacks.

8. Many asthmatic persons have difficulty in deciding to marry.

9. After allergic patients have succeeded in overcoming their emotional conflict regarding emancipation from the mother or mother figure, they become more resistant to allergens.

10. The threshold for allergic sensitivity is dependent on the emotional state of the patient.

The therapeutic result in the study by French and Alexander is difficult to evaluate, for at the time of reporting, some of the patients were still under treatment and others had not been observed over a sufficient period of time. Of 19 patients who were under treatment six months or more, nine were symptom-free and eight were improved. Those treated for a shorter period of time showed improvement.

French and Alexander⁵ discussed the observations of Siegfried Burnfeld of eight asthmatic children over a ten-year period. Burnfeld's conclusions as to the personality of the mother of the asthmatic child were quite in agreement with those reached by French and Alexander—that she is somewhat more critical of and less interested in her child than the "average" mother. At the same time she is observed to have a close bond with the child. She is more worrisome and tense than the average.

Part II of the monograph is a series of detailed case reports.

In a chapter on bronchial asthma in "Psychosomatic Medicine" by Weiss and English published in 1945, a chapter that is essentially a review of the monographs just mentioned plus a brief summary of the literature, Weiss concluded that attacks of asthma develop as a reaction to separation from the mother (or mother figure) and are comparable to the shrieking of a helpless newborn child. He interpreted this behavior of the newborn as a protest against separation from the mother and expressed belief that attacks of asthma are a recapitulation of this experience.

In a series of papers⁵ Hyman Miller, an allergist, and Dorothy Baruch, a psychologist, reported their attempts to coordinate medical treatment and psychotherapy. They concluded that maternal rejection is an important item in the emotional climate of an

allergic child's environment; that allergic symptoms can represent attempts to gain sympathy, express hostility and to mask a feeling of guilt or anxiety; and that the release of emotions in psychotherapy is paralleled by a decrease in symptoms.

To summarize: The literature stresses that attacks of asthma are associated with a variety of emotional conflicts. Asthma has been considered to be owing to:

1. Conversion hysteria; basic anxiety hysteria.
2. A reflex neurosis; a secretory neurosis; a central or bulbar neurosis; a compulsion neurosis.
3. A conditioned reflex mechanism.
4. Rejection by the mother. This last theory has, of recent years, received more publicity than any of the others. Since the public has been made more aware of psychiatry and psychiatric problems, the rejection-by-mother contention has caused much disturbance in families of allergic children.

It cannot be denied that rejection of a child by the mother or father or siblings, or of a husband or wife by the spouse, can occur. However, isn't it more sensible to consider the rejection as the result rather than as the cause of the allergic disease? The prolonged expense of medical care, making it necessary for other members of the family to sacrifice necessities or little luxuries; the extra work involved in preparing special diets; disturbed sleep caused by the crying or coughing, may all lead to resentment against the patient and eventually to rejection. The situation may be quite similar in any other prolonged illness such as diabetes, nephrosis, or malignant disease.

Much of the literature has been written by psychoanalysts. Even if psychoanalysis were to be proved and accepted as the therapeutic procedure in the treatment of allergic disease, particularly asthma, it would still be most impractical owing to the long period of time required and the prohibitive cost. Also there is the concept that any admission of a psychogenic problem is a social stigma, and many patients would resent being referred to a psychiatrist.

Probably most physicians agree that psychological problems play an important role in the production and exacerbation of medical difficulties, especially in medical problems of a chronic nature that entail economic and social problems. Common sense and a certain practical knowledge of life enable experienced physicians to comprehend the patient's personal problems in relation to his illness. Since a physician is in a position of influence and authority, what he says and does is important to the patient.

Some patients make satisfactory progress with whatever treatment a physician outlines. Some patients are so pliable and capable and have so much nervous stability that they come through the most uncomfortable illness and the most adverse situa-

tions undamaged. Some do not, and it is they who can be helped by a physician's taking a little extra time to investigate and rebalance their mental environment.

"The relative degree and significance of allergic and emotional factors should be determined and the patient treated accordingly," Wittkower⁷ said. "In some patients, emotional factors are of minor importance, in others they deserve serious consideration, and in still others they are all-important. Therefore, the physician should treat the patient and not his allergy alone."

For that reason sufficient time should be allowed for taking adequate history, including a life history. A few simple questions such as, "Are you happy?" or "Are you worried about anything?" often bring forth a great amount of information. There may be some physicians who feel they do not have sufficient psychologic understanding or training to give adequate care to patients with illness in which emotional disturbance plays a large part. However, such training is now available at a number of places.

The author does not have "psychotherapeutic sessions" apart from the regular desensitization treatment, but if a patient does not make satisfactory progress, he is invited to "talk things over." The patient is pleased with the extra attention, and it takes very little questioning as a rule to locate an emotional problem. By the next visit the patient usually decides to unburden himself completely. A few additional periods of consultation are usually sufficient.

Deep psychotherapy or analysis is necessary for a very small proportion of patients, the incidence being no greater in patients who have allergic disease than it is in any other patients.

The therapy of choice for all patients with allergic disease should be that method or combination of methods which will produce for the patient most effectively and economically the optimum in health and personal and social efficiency.

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Female Infertility

The Present Status of Treatment

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OF THE MANY WOMEN who consult a physician because of infertility, only a small proportion have important pelvic disease, and rarely do basal metabolic rate determinations, hormone assays, or other laboratory studies give a clue to any abnormality that would prevent pregnancy.

Many apparently normal women have one or more of the frequently encountered gynecological abnormalities such as endocervicitis and erosion, simple retroversion, fibroid formation, infantile uterus; but such conditions probably are not important factors in infertility. Some erosion or endocervicitis was noted in more than 60 per cent of several hundred women in routine examinations of the cervix in early pregnancy. Retroversion was also observed at the initial examination in about one case in five. Fibroid tumors are not uncommon. In the author's experience pregnancy seems to occur in an infantile uterus about as readily as in one of normal size.

Such abnormalities therefore may be looked upon as coexisting conditions rather than as causes of infertility, yet attention must be given to them in any general program of treatment of a patient who wishes to become pregnant.

After years of observation and study, the actual causes and the solution of barrenness in women who seem to have no abnormality sufficient to prevent pregnancy continue to be as much a mystery as ever. So far all that can be said is that pregnancy follows the use of some drugs and some instrumentalities often enough to escape the label of coincidence.

Many drugs have been used, among them endocrine substances. Presumably, the glandular system governs ovulation, the quality of the ovum, the potential attractiveness of the ovum to spermatozoa and the preparation of the bed for implantation.

After long experience with attempts to overcome sterility by use of drugs most clinicians favor desiccated thyroid. Presumably it is a general glandular stimulant or tonic and should affect any or all of the phases mentioned. The prevailing practice is to increase the dosage to tolerance rather than to attempt to determine, on the basis of the basal metabolic rate, the amount needed in each case.

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• Few barren women have gynecological abnormalities sufficient to prevent conception. Hormonal stimulation appears to be effective in some cases; and sometimes pregnancy follows instrumental treatment, possibly as a result of dislodgement or displacement of polyps in the process. There is nebulous evidence that psychogenic factors may play a part in infertility.

If the fallopian tubes are occluded, operation to restore patency is not likely to clear the way to conception.

If administration of desiccated thyroid is ineffective, attempt may be made to enhance the process of ovulation by giving the patient anterior pituitary products, although such substances if not entirely disappointing certainly are not as effective as, theoretically, they should be. Estrin and progestin, administered hypodermically or orally, have given as much encouragement if not more, even though theoretically they would seem to offer less.

Even though the patient keeps a careful basal temperature chart, often there is some question as to the time of ovulation. In that event cytologic study of vaginal secretion may be carried out or, more conclusive, endometrial biopsy.

A factor to be considered is the possibility of ovulatory depression followed by rebound stimulation by pituitary activity—that is, the parallel in women of the pattern observed by Heller in studies of spermatogenesis. It is not unusual for a woman to become pregnant a few months after she has discontinued all treatment in disgust.

The gonad-liver-pituitary syndrome and nutritional and liver therapy under investigation by Glass continues to look promising.

Results of various types of vitamin E and vitamin C therapy, after several years of routine use, are not such as to warrant use of the substances to promote fertility.

As there is known to be considerable fluctuation of the fertility index in males, it may be assumed that in females there is a similar variation even though there is no way to observe it as there is in

males. Investigations of drugs are justified, therefore, even though there is no method of proving by direct observation what effect they have on fertility in women.

Many previously barren women became pregnant after instrumentation treatment of one kind or another—tubal insufflation, endometrial biopsy, dilatation and curettage, cauterization of the cervix, or a simple probing of the cervical canal. Various explanations have been given for these successes.

The most reasonable came from Holman, of Portland, who noted in hysterosalpingographic studies that a considerable proportion of patients had polyps at the internal os. Removal or displacement of polyps by instrumental treatment could very well remove some kind of mechanical barrier or change a biologic process that inhibited pregnancy. It seems reasonable to assume even though polyps are not present there still might be granulations that would have the same effect. Perhaps that is why in some cases the cervical canal bleeds so easily when probed.

Almost all physicians interested in fertility must now and again have occasion to meditate upon psychogenic factors. For example, the classic case of a man and wife who have had all known treatment without success and finally adopt a baby. Then soon afterward the wife may become pregnant. Statisticians are trying to prove such occurrences to be coincidence, but the arguments seem pretty thin. Physicians must wonder if there is not in such cases

a psychogenic barrier that yields when parenthood becomes a fact. Or does some glandular change take place? Perhaps some unknown response to a little baby completely dependent upon the couple who adopt him stimulates a more efficient gonadotropin than can be put into a tablet or a syringe. Pregnancy occurring at the "change of life" after long barrenness is hard to explain except on the basis of glandular change, and it must be wondered if perhaps the same change could have been achieved earlier by more efficient and tenacious management.

There is no way to demonstrate whether there is or is not biologic antagonism between the ova of one person and the sperms of one other. But there is reason for conjecture. It is not uncommon for a childless couple to divorce and then each have children with a new spouse. And what of sterility after the birth of one child? Could antagonism develop and replace the necessary attraction-force? Recently the author delivered a patient of her second child. Each was conceived by artificial insemination with donor semen. However, although three attempts were made to impregnate the woman the second time with semen from the same donor who had been used in the first insemination, conception did not occur. Semen from another donor then was used and pregnancy resulted.

If the fallopian tubes are occluded there is little likelihood that an operation to restore patency will clear the way to conception.

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Diaphragmatic Herniation Through the Space of Morgagni

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DIAPHRAGMATIC HERNIA is a general term denoting protrusion of viscera through an abnormal defect in the diaphragm. Such hernias are classified as congenital or acquired and traumatic. A hernia is regarded as congenital if present at birth or developing gradually after birth in a congenitally weak area. With few exceptions congenital diaphragmatic hernias have a peritoneal sac.^{5, 6, 8} Traumatic hernia results from a penetrating injury, from tearing of the diaphragm by violent abdominal or thoracic compression, or from necrosis secondary to an inflammatory process. It does not usually have a peritoneal sac.⁹

As normally formed, the diaphragm is a single dome-shaped muscle that divides the thoracic and abdominal cavities and is traversed only by the esophagus and the inferior vena cava. (The aorta passes posteriorly.) In adults the muscular portion is divided into three parts, sternal, lateral and lumbar, named according to origin, and all are inserted into the margin of the central tendon. The sternal portion consists of a few bundles of muscle arising from the xiphoid process. The muscular deficiencies on either side of the sternal portion, filled by areolar tissue, carry the superior epigastric vessels. These deficiencies are called the "spaces of Morgagni."

The occurrence of herniation of abdominal viscera through these foramina has been known for many years. Morgagni, the Italian anatomist, is credited with the first description of such a hernia, in 1769. It was observed in a patient who died of other causes at an advanced age and in whom herniation of intestine (without obstruction) into the thoracic cavity through such an opening was found at autopsy. No sign of injury to the diaphragm was noted.⁴

During embryonic development many changes occur simultaneously which account for the possibility of diaphragmatic hernias.^{3, 5} These changes consist of multicentric formation of the diaphragm and rotation of the gastrointestinal tract with a shift of the liver to the right and presence of hollow mobile viscera on the left side. The septum transversum de-

scends rapidly from the cervical region (phrenic nerve innervation) to occupy an anterolateral position; a mesodermal shelf, the "pleuroperitoneal membrane," descends with the septum transversum to occupy and close the posterolateral position of the diaphragm; and the dorsal mesentery forms the posterior and central portions which contain the esophageal opening.

If diagnosis is established, thoracotomy is indicated as an elective procedure for repair of the defect, which may have serious consequences.

Nine cases of diaphragmatic herniation through the space of Morgagni are summarized and a case report is included which illustrates the potential danger of this condition.

scends rapidly from the cervical region (phrenic nerve innervation) to occupy an anterolateral position; a mesodermal shelf, the "pleuroperitoneal membrane," descends with the septum transversum to occupy and close the posterolateral position of the diaphragm; and the dorsal mesentery forms the posterior and central portions which contain the esophageal opening.

When a hernia is acquired after birth it usually has a hernial sac and occurs most frequently at the esophageal hiatus, next often at the pleuroperitoneal hiatus (foramen of Bochdalek), and least often at the foramen of Morgagni. In the series collected by Hedblom (728 cases)⁶ and by Harrington (524 cases),⁹ only about 6 per cent of non-traumatic diaphragmatic hernias occurred at the foramen of Morgagni. True congenital hernia is of no higher incidence in one sex than in the other, but the acquired type occurs preponderantly in females. Acquired hernias probably develop because of increased intra-abdominal pressure as in pregnancy, labor, straining at stool, coughing or vomiting. Major contributing factors are weakening of the diaphrag-

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matic muscle and absorption of fatty deposit between the serous membranes.⁶

Acquired hernia is not to be confused with diaphragmatic eventration in which large areas of the diaphragm become weakened and elevated. Such irregularities of the diaphragmatic leaf are common and, unless quite pronounced, can be classified as within normal limits.

There is no characteristic symptom or syndrome of diaphragmatic hernia. Often hernia of the foramen of Morgagni is asymptomatic and is noted in a routine chest x-ray survey. Symptoms vary from mild respiratory distress to repeated attacks of intestinal obstruction, depending on what organs are displaced. If only omentum protrudes, the discomfort is usually minimal, in some cases no more than mild respiratory distress such as dyspnea or cough. Large hernias may lead to more severe respiratory symptoms, and in children may cause death from respiratory embarrassment.³ If the stomach or the small or large intestine protrudes there may be a wide range of symptoms including nausea, vomiting, sense of bloating or fullness after eating, epigastric pain or discomfort, abdominal distention and colicky pain. Such combined symptoms of respiratory and gastrointestinal disturbance frequently are confusing and lead to erroneous diagnosis. Harrington⁵ stated that the very protean nature of the symptoms is most characteristic of diaphragmatic hernia.

Failure to recognize and properly attribute symptoms of herniation through the space of Morgagni has serious potentialities. The literature contains reports of occasional cases of death from intestinal obstruction in all age groups.^{1, 3, 5, 6} The following case represents such a missed diagnosis:

CASE REPORT

A 50-year-old white man was admitted to hospital in October 1950 with the chief complaint of abdominal pain of 24 hours' duration. He stated that he had been in fairly good health until 5:00 p.m. the previous day, when he had sudden, severe pain high in the epigastrium, with continuous vomiting. The pain shifted to the periumbilical area and remained there. The patient had had intermittent sensation of bloating with belching and occasionally passed flatus.

On physical examination the patient was observed to be obese and of florid complexion; he sat erect in bed and obviously had abdominal distress. The temperature was 99.8° F., the pulse rate 100 and respirations 28 per minute. Blood pressure was 170 mm. of mercury at systole, 100 mm. at diastole. The abdomen was moderately distended; hyper-resonance and tenderness in the lower epigastrum and umbilical area were noted, but there was no guarding, rigidity or rebound tenderness, and peristalsis was active. No masses were palpated.

Hemoglobin in the blood measured 15.4 gm. per 100 cc. and leukocytes 8,900 per cu. mm.—84 per cent polymorpho-nuclear cells and 16 per cent lymphocytes. The urine appeared to be normal.

The tentative diagnosis was subacute pancreatitis; and a

conservative regimen of fluids intravenously administered, penicillin, and Demerol® was begun. During the afternoon of the second hospital day further pain developed, most prominent in the right lower chest and more pronounced on respiration. The right lower chest was dull to percussion and breath sounds there were diminished. In a roentgenogram of the chest the diaphragm was observed to be elevated on the right side and there was a large area of decreased density beneath which there appeared to be localized gas. This condition was considered compatible with subphrenic abscess. Supportive therapy was continued but the patient's condition gradually and progressively deteriorated and he died on the ninth hospital day. No definite diagnosis had been made.

At autopsy the right side of the thoracic cavity was found to be filled by herniated gangrenous perforated ascending and transverse colon strangulated and obstructed at the foramen of Morgagni.

The diagnosis of diaphragmatic herniation through the space of Morgagni can be suspected if a lateral roentgenogram of the chest shows shadows of the lower lung field at the cardiophrenic angle lying far forward and not entirely within the thorax. (The importance of lateral view x-ray films in localization of lesions of the chest cannot be overemphasized.) After a barium meal portions of the gastrointestinal tract may be seen within the hernia. It has been pointed out that an inverted "U"-shaped or "V"-shaped deformity of the transverse colon may indicate omental hernia.⁷ The advantage of pneumoperitoneum as an aid to diagnosis has been previously emphasized.¹⁰ This procedure will usually permit visualization of the hernial sac, but incarceration of omentum may in some cases prevent filling of the sac with air and lead to an erroneous interpretation.

A mass at the anterior cardiophrenic angle may be lipoma, lymphoma, teratoma, neurofibroma, pericardial cyst, tuberculoma, or a peripheral lesion of the lung, perhaps carcinoma of the middle lobe. Exploration should be considered early when diagnosis cannot be established by simple measures; a long period of observation of roentgenographic shadows is not consistent with modern medical standards.

The thoracic approach permits the best exposure of diaphragmatic hernia^{2, 11} and also facilitates examination of the entire contents of the hemithorax for undiagnosed lesions. A diaphragmatic defect can be enlarged if necessary to provide excellent exposure of the upper abdominal contents. Any adhesions of the herniation to thoracic contents can be readily separated under direct vision, and repair of the defect can be made with a minimum of tension on surrounding tissues. The upper abdominal approach may possibly be advantageous in bilateral herniation of Morgagni.

Of the nine cases of diaphragmatic herniation through the space of Morgagni in adults that are summarized in Table 1, six were repaired successfully with thoracotomy. In one of the other three cases operation was precluded because of advanced

TABLE 1.—Diaphragmatic Herniation Through the Space of Morgagni

Age	Sex	Symptoms	Diagnostic Procedures	Date of Operation	Hernial Contents	Remarks
41	F	Mild chronic cough	Routine chest x-ray; bronchoscopy and bronchograms negative	1-6-48	Omentum	Cough unchanged
48	F	Occasional shortness of breath	Routine chest x-ray; barium enema negative; bronchoscopy negative	3-24-48	Omentum	Markedly obese
50	M	Acute severe epigastric pain	Missed	None	Perforated obstructed transverse colon	No operation; diagnosis made at autopsy.
54	F	None	X-ray with pneumoperitoneum; bronchoscopy negative	None		Mistaken for middle lobe lesion. Advanced generalized arthritis prevented operation.
56	F	None	X-ray with pneumoperitoneum; routine chest x-ray	Refused		Operation refused.
24	M	Mild, life-time anterior chest discomfort, aggravated by deep breathing or food	Upper gastrointestinal series, barium enema, x-ray with pneumothorax and pneumoperitoneum: all negative	7-31-51	Omentum	Superficial wound sinus healed after two months.
44	F	None	Routine chest x-ray	9-10-51	Omentum	Vague discomfort, preoperatively disregarded, relieved.
52	F	None	Routine chest x-ray	10-16-51	Omentum	
38	F	Cough and mild lower chest pain, vague epigastric distress after meals	Routine chest x-ray	3-28-52	Omentum	

systemic disease, and in another operation was refused. In the third, reported above, the patient died before diagnosis was made. In all nine cases shadows were observed in the right cardiophrenic angle in routine x-ray films of the chest. Most of the patients had minimal or no symptoms. Herniation was suspected from conditions observed in fluoroscopic examination and x-ray films of the chest. Pneumoperitoneum was an important adjunct in diagnosis in the two cases in which operation was not done. The following case report is illustrative:

CASE REPORT

A 48-year-old white married woman was referred by a physician in March 1948 for study of a suspected tumor of the chest. Routine chest x-ray films had been made because of occasional shortness of breath and fatigability. The weight of the patient had increased from 180 to 200 pounds in a short time.

On physical examination she appeared to be in good health. Except for obesity no serious abnormalities were noted. On fluoroscopy and x-ray films of the chest a large mass, about 10 cm. in diameter, was observed at the anterior cardiophrenic angle. No abnormality was noted in roentgen study of the upper gastrointestinal tract.

Thoracotomy was done two weeks later. A portion of omentum was found in a large sac and was excised. A diaphragmatic defect of the space of Morgagni was repaired. Convalescence was uneventful.

SURGICAL MANAGEMENT

The authors prefer to use endotracheal anesthesia for the operation. The diaphragm is exposed through an anterolateral incision in the sixth intercostal interspace. Transpleurally the hernial sac and its contents can be well visualized. The contents are replaced into the abdomen and the defect closed with interrupted sutures. The chest is closed tight over a catheter which is withdrawn as the last suture is tied while the anesthetist exerts positive pressure to ensure complete expansion of the lung.

Postoperative care consists of prophylactic use of antibiotics, early ambulation and early feeding. Nasal oxygen is administered until the patient recovers from anesthesia. The patient may sit on the edge of the bed in the evening after operation and can usually be discharged from the hospital about the fifth postoperative day, when he is able to be up for meals and for lavatory purposes. Demand feeding seems to be advantageous, and as a full regular diet is usually taken by the second postoperative day, intravenous feeding is rarely indicated. Mild analgesia to control pain without depressing the cough reflex is important. A roentgenogram of the chest is routinely made before discharge from the hospital to check lung expansion and pleural effu-

sion. The cases here reported were not complicated by failure of lungs to expand or by collection of pleural fluid; if these occur thoracentesis may be done. The patient is allowed to return to his former duties within a month after operation.

The results of the operation have been satisfactory and without pleural complications or recurrence of hernia. Intercostal pain is largely prevented by the injection of xylocaine in oil along the intercostal nerves at operation. Patients usually have mild pulling sensations in the lower part of the chest for about two months postoperatively, but rarely is this severe enough to necessitate blocking of intercostal nerves.

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Questionable Compensation Claims

Principles of Special Examination

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THE LARGE MAJORITY of industrially incurred injuries are minor in nature, the employee returning to work fully recovered with no permanent disability. A certain number of industrially injured employees, however, continue as totally disabled much longer than the attending physician has estimated, or later present complaints and conditions not originally anticipated. In the treatment of such patients it is often necessary to obtain one or more complete medical evaluations to determine the relationship of a patient's complaints and disorders to the original injury and to understand the case from multiple standpoints. Such a reevaluation is called a special examination, and this examination is usually made by specialists in various fields. When a physician is asked by an insurance carrier to make a special examination on a questionable compensation claim, it is obvious that a conflict or problem has arisen, or there would be no need for such special examination. He should therefore know the point of contention, and obviously he should be conversant with all facts pertaining to the case from the time of injury up to the time of special examination.

Physicians have been accused of being "prima donnas," and there appears to be a certain amount of truth in that charge, for practically all physicians who treat industrially disabled persons consider themselves very well qualified to do so. Further, the large majority of physicians to whom patients are sent for special examinations consider themselves thoroughly equipped to render accurate opinions as to the status of questionable compensation claims. Having personally reviewed the reports of many examining specialists covering a large number of questionable compensation cases, the author does not agree that all physicians, by the very fact that they are specialists in their fields, are competent authorities in the evaluation of industrial injuries. Too often an industrially injured patient is regarded only as a patient, with no consideration of the many extraneous factors which might tend to perpetuate complaints.

The author has read many reports in which a history of an injury of long duration is no more than

*• In deciding a disputed claim of disability arising from occupation, physicians should ascertain whether a patient's medical history has any bearing on the disability; they should attempt psychologic evaluation of the patient as it may reflect on the conditions they observe in physical examination; they should investigate symptoms complained of by the patient rather than accept them as *prima facie* evidence of disability; and they must have knowledge of the extent to which an injury can cause disability.*

It is urged that standards of physical ability and disability, as well as of other physical factors which may affect compensation claims, be established by organized research.

15 or 20 typewritten lines. In many reports, too, there was no past medical history and therefore no indication as to whether such history might have a bearing upon the patient's present complaints. Rarely is a personal evaluation of the patient included in the report of the special examination and even more rarely is an opinion given of the patient from a psychologic standpoint, with an evaluation of the many stresses and strains, both family and economic, which might have an important bearing upon the case. An evaluation of the patient's ability to work, taking into consideration his complaints and disabilities, is omitted in many reports or, if given, does not indicate the type of work which the patient can perform or the date upon which he will be able to return to work. The physical examination is, as a rule, competently done, but at the point where the information obtained by interrogation and by examination must be evaluated, the special examiner often fails in his duty.

The special examiner of a questionable disability claim sits in much the same capacity as a judge in a trial. Evidence is presented, both through interrogation and through examination, which has a definite bearing upon the patient's continuing complaints. It is incumbent upon the examiner that he fairly weigh all the evidence and upon this evidence arrive at an exact conclusion.

It may be protested that medical science is an inexact science and therefore that it is asking the im-

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possible to suggest that a physician should arrive at an exact conclusion based upon examination. But is not the judge or jury at a trial, be it civil or criminal, forced to weigh the evidence pro and con and arrive at an exact conclusion? There is surely no more exact conclusion than the sentence of death, which is based entirely upon evidence presented and weighed. Physicians have too long hidden behind the defense that medicine is inexact and that therefore they should not be called upon ever to render a final and conclusive opinion unless allowed to protect themselves by including as an adjunct to that opinion many other medical possibilities.

It is quite possible that an examiner may err when attempting to arrive at an exact conclusion regarding a disability. Nonetheless, it is incumbent upon him to arrive at a conclusion, which it is his responsibility to substantiate. It is not the practice of insurance carriers to attempt to influence this conclusion in any way, but they are at an absolute loss to carry out their obligation in the care of the industrially injured without medical opinion. It naturally follows that if a medical opinion is ambiguous and full of loopholes it is of no value to the carrier, who rightfully wants to know whether a patient's continuing complaints are real, whether they are related to his original injury, whether the accident as described by the patient could have possibly produced the condition ascribed to it, and many other facts relating to the claim. Whether the conclusion is favorable to the carrier or to the patient should be of no importance to the examiner. The author has often heard the opinion expressed by claims agents for insurers that they would much rather see a report with a definite conclusion which "sticks them" than an ambiguous report and a loose conclusion which "lets them off the hook."

An example of deficiency in this regard was in the case of a man who received a minor injury at work but had a protracted period of temporary total disability based upon the complaint of pain in the neck. A special examination was carried out and the report based upon the examination was full and complete: In review of the history and in the physical examination it was clearly demonstrated, from a medical standpoint, that there was no basis in fact for the patient's continuing complaint and his continuing allegation that he could not work. But the concluding paragraph stated, "Of course it is possible that this patient may have some condition present which I have not been able to find by examination and therefore I would suggest that he be hospitalized and cervical traction instituted to determine whether this treatment will have any effect upon his complaints." Although the entire body of the report demonstrated clearly that in the examiner's mind the patient had no disorder and no rea-

son not to work, his last paragraph completely negated the entire report for insurance purposes and made it obligatory on the insurer to continue treatment and compensation payments in spite of the fact that no cause of disability was found.

RELATING SYMPTOMS TO CAUSE

Examiners of the industrially injured must become more medically suspicious and must not accept symptoms reported by the patient as *prima facie* evidence of the presence of disease or injury. Further, when a complaint is compatible with a finding of abnormality it must be demonstrated that the abnormal finding did arise from the stated injury. It is not sufficient to assume, because a patient gives a history of injury and presents complaints relative to an allegedly injured portion of his body and a pathologic condition is found there, that the condition must therefore have arisen as a result of occupation as contended by the patient.

An excellent example of the error in such *ipso facto* thinking in medicine was presented by Kirkpatrick.¹ He stated that when a person finds himself suddenly incapacitated he can usually recall some unimportant incident upon which to fix the blame for the condition. It is quite common for laymen to rely on the "must-have-been" diagnosis. In many instances the physician who first sees the patient unwittingly falls into the same kind of error in trying to arrive at a diagnosis and informs the patient that he "must have" bumped himself. Detailed questioning in cases connected with occupational disability seldom elicits any admission of prior symptoms of any kind, since the patient immediately senses the object of the questioning. Kirkpatrick pointed out that in a series of 100 cases (reported in 1928) in which gout was a factor, 88 per cent of the physicians who had previously examined and treated the patients had not recognized gout as the underlying cause of the complaint; in another series of 100 cases reported in 1946, nearly 50 per cent of the physicians had failed to recognize gout as a cause of disability. An acute attack of gout has its inception several days before the acute symptoms are evident. Therefore, gouty bursitis or periarthritis which is first noticed in the course of a person's usual work should not be considered industrially connected or aggravated. It is obvious that unless the examiner is medically suspicious during the conduct of a special examination a condition such as gout can be easily overlooked and the patient's complaints and abnormalities attributed to trauma arising from injury rather than from a disease process which has no relationship to occupation.

Certain errors in the evaluation of disability due to industrial injury result from a lack of standards

for measurement. For example, one of the most common procedures in the examination of the industrially injured is a determination of the patient's grasping power. Unfortunately there is little standardization either in the method of carrying out this study or in interpreting it. Nemethi² reported that in preemployment physical examination of 1,000 persons aged 18 to 65 years it was found that the difference in grasping power between the major and the minor hand was 5 per cent in men 25 to 30 years of age and 15 per cent in men aged 30 to 35 years, while in women the difference was 25 per cent. The tests were made with a standard spring gripping mechanism. Although there were several factors in the conduct of this study on which the author disagrees, such research is pointed in the right direction. It is generally assumed that the major hand has a grasping power of 10 per cent in excess of the minor hand. Nemethi's study indicates that this assumption may not be based upon fact. Some standard for estimation of grasping power is absolutely necessary for proper evaluation of injuries.

Medical examiners must have standards for injured as well as for normal hands. In one case, in which the entire injury was the loss of the thumb of the major hand at the distal joint, the grasping power of the major hand, as determined when the condition was considered static and ready for rating, was shown as 50 per cent of the grasping power of the minor hand. The examining physician did not possess a knowledge of values for injured hands; to him a decrease in grasping power of 50 per cent was compatible with the injury. To those who have made extensive examinations of grasping power, however, such a loss of gripping power is far greater than could be incurred by injury of that type.

Atrophy of the arm or the forearm, the thigh or the leg is often reported in medical examinations. As an example, if the circumference of the normal

and major right mid-arm is found to be 13 inches and the circumference of the injured left mid-arm is found to be 12 inches it is reported that atrophy has reduced the left arm by one inch. The author questions whether in such a case atrophy is really present or whether there is not in fact a normal difference in circumference between the opposite extremities. Such a difference, if it exists, apparently is not known, but the question seems worthy of investigation. It is suggested that the California Medical Association assume the responsibility, as it did in preparing the book "Evaluation of Industrial Disability," of determining a set of standards to assist in measurements of industrially injured patients. This would be a laborious task, but it would make for more accurate medical reporting.

Examining physicians must recognize their duty to consider only the medical aspects of each case, being totally impartial to both the patient's and the insurance carrier's interest. They must be careful, when a contention on the part of the patient is not medically justifiable, not to provide inadvertently the doubt upon which all benefits can be granted to the patient.

It is to be hoped that in the future the ambiguities seen so often in the past reports will be avoided and that examiners will have the courage to state their opinions honestly without placing in their reports substitute or contrary opinions merely to protect themselves in the event that they might be wrong. The physician ought never try to avoid the duty of making up his mind.

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CASE REPORTS

• New Therapy in a Case of Tetanus

New Therapy in a Case of Tetanus

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A SIXTY-FOUR-YEAR-OLD well-nourished white man who weighed 195 pounds entered the hospital on June 21, 1952, complaining of inability to open his mouth. He stated that a splinter had entered the base of the left thumb seven days earlier and that bilateral stiffness of the jaw was first noted on June 20.

Upon physical examination symptoms typical of a mild case of tetanus were noted; the abdominal muscles were in a sustained spastic state and the jaws were locked. The wound of entrance was debrided. *Clostridium tetani* grew in a culture. Plasma electrolytes were in normal balance and the patient was given chloral hydrate for sedation for three days, then Resyl® was added. The following day, he could open his mouth, but later in the day tracheotomy was done to bypass hypopharyngeal secretions accumulating because of laryngospasm. The following day the patient was breathing very much better and sedation was limited to diminished doses of Resyl. That evening a severe convulsion occurred and the dosage of Resyl was increased. The effect the following day, June 27, was dramatic. The abdomen was much relaxed and the patient could open his mouth quite wide fairly easily, but feeding through a Levine tube was continued. Contractions of variable severity continued through July 13, 1952 (see Table 1).

There was no bowel movement from June 21 to July 13. Numerous enemas were given, then magnesium sulfate was administered July 11, 12 and 13 and the patient had three movements at which semiformed or liquid stools were passed. The condition of the patient was much better from then on although insignificant muscular contraction occurred from time to time until July 21, after which he was convalescent. X-ray films of the vertebra showed compression fracture of the T 12 without symptoms.

During the period of hospitalization the leukocyte content of the blood varied from 8,800 to 15,000 per cu. mm., with polymorphonuclear cells predominating. On July 4, the urine showed only an occasional erythrocyte, although it was amber to light red in color. On July 7, one specimen caused moderate reduction of Benedict's solution.

The patient was discharged July 31, 1952, with no additional therapy prescribed.

COMMENT

If penicillin can reach the tetanus organism within the body, theoretically it should destroy it. Nevertheless, where the focus of infection is known and can be removed surgically, this should be done after afferent pathways between it and the central nervous system are blocked with injected antitoxin. While it is presumed that antitoxin can combine

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only with circulating tetanus toxins not yet bound by nervous tissue, and that small doses should suffice, the author's practical experience (more than 30 years of observing numerous cases of clinical tetanus) has taught that patients do not recover unless they receive substantial doses of antitoxin, theory to the contrary notwithstanding. Patients with the disease rarely survive if doses less than 100,000 units are received. While the optimum dose of antitoxin must vary with the individual, in observation of several hundred cases, the author has noted that as a rule the dose should be not less than 120,000 units or more than 350,000 units, preferably given in the first 24 hours of treatment.

Skin testing for sensitivity to antitoxin affords reliable information only when the result is strongly positive; negative results are unreliable and may lead to a false sense of security. The intravenous blood pressure test appears to give the most reliable information of the various tests used. In this test 0.1 ml. of antitoxin is diluted in 10 ml. of normal saline (never dextrose) solution which then is slowly injected intravenously. The blood pressure is recorded before injection and every five minutes for 30 minutes thereafter; if it falls 20 mm. of mercury or more, the patient is sensitive, and he must be desensitized before receiving antitoxin. If haste is urgent, the patient may receive 20 mg. of heparin intravenously per kilogram of body weight,⁵ and then the antitoxin may be given at once without desensitizing; but after 18 hours, if antitoxin is to be given again, it is necessary to give heparin again. Naturally, heparin should not be used if there is danger of hemorrhage.

The classic theory of Meyer and Ransom,⁶ that the muscular rigidity in tetanus is owing solely to the poisonous effect of the tetanospasmin component of tetanus toxin upon the nerve centers within the central nervous system, appears to be no longer tenable, since Harvey^{7,8} found that the motor end apparatus itself is poisoned in localized tetanus. He postulated that this was caused by inactivation of cholinesterase which increased the acetylcholine, manifesting itself electrophysiologically by intermittent discharges at the end plate. Goepfert and Schaefer⁹ found that the continuous muscular spasm resulting from these stimuli was the cause of opisthotonus, rigid abdomen, risus sardonicus, and trismus.

Thus, while patients require antitoxin to survive, this alone is insufficient to save life. Two additional procedures are indicated: sedation adequate to prevent death from severe convulsive seizures, and the maintenance of an unobstructed airway with an exchange of respiratory gases adequate to maintain life.

The problem of sedation in tetanus is a complex one. Until the advent of mephenesin (3-ortho-toloyl-1,2-propanediol) and of the various standardized extracts and alkaloids of curare, sedation was purely symptomatic and was induced solely through the continuous and prolonged use of hypnotics, narcotics, or anesthetics—for example, chloral hydrate and barbiturates. These drugs first produce a depressive effect on the cerebral centers and then, depending upon the depth of narcosis, descend to lower cord levels through

TABLE 1.—Medication of a Patient With Tetanus

Date in 1952	Chloral Hydrate in grains	Resyl					Antibiotics				Units of tetanus antitoxin
		Intravenous		In grams			Penicil- lin in millions of units	Crysacillin in numbers of 300,000 unit injections	Chloram- phenicol in mg.		
		Ml.	Per cent Sol.	Intra- venous	Oral	Total					
June 21.....	30	—	—	—	—	—	5	—	—	120,000*	
June 21.....	—	—	—	—	—	—	—	—	—	40,000†	
June 22.....	225	—	—	—	—	—	10	—	—	—	
June 23.....	270	—	—	—	—	—	—	—	—	—	
June 24.....	240	—	—	—	—	—	5	—	500	1,500*	
June 25.....	60	500	5	25.0	—	25.0	—	—	2,000	—	
June 26.....	90	600	5	30.0	—	30.0	—	—	500	—	
June 27.....	120	640	5	32.0	—	32.0	2	—	—	40,000*	
June 28.....	250	10	5	—	—	—	—	—	—	—	
June 28.....	—	2,000	1	—	—	—	—	—	—	—	
June 28.....	—	290	3	—	—	—	—	—	—	—	
June 28.....	—	650	½	32.4	—	32.4	2	—	—	—	
June 29.....	180	1,750	1	—	—	—	—	—	—	—	
June 29.....	—	2,080	2	—	—	—	—	—	—	—	
June 29.....	—	190	3	64.8	—	64.8	2	—	—	—	
June 30.....	190	1,400	1	—	—	—	—	—	—	—	
June 30.....	—	800	2	30.0	8	38.0	2	—	—	1,500*	
July 1.....	150	550	2	11.0	20	31.0	2	—	—	—	
July 2.....	210	800	2	16.0	22	38.0	1	1	—	—	
July 3.....	180	1,000	2	20.0	24	44.0	—	5	—	1,500*	
July 4.....	210	1,125	2	22.5	24	46.5	—	3	—	—	
July 5.....	300	1,225	2	24.5	24	48.5	—	4	—	—	
July 6.....	300	800	2	16.0	24	40.0	—	4	—	1,500*	
July 7.....	210	1,000	2	20.0	24	44.0	—	5	—	—	
July 8.....	330	850	2	19.5	—	—	—	—	—	—	
July 8.....	—	50	5	—	24	43.5	—	3	—	—	
July 9.....	240	500	5	25.0	16	41.0	—	4	—	1,500*	
July 10.....	300	550	5	27.5	18	45.5	—	3	—	—	
July 11.....	60	—	—	—	—	—	5	2	—	—	
Total.....	4,165	—	—	416.2	228	644.2	36	10.2	3 grams million units	207,500 units	

* Intramuscularly. † Intravenously.

the thalamus and medulla. It is really at this last site, not the former, that the soothing or paralytic therapeutic effect upon the interneuronal fibers is specifically desired, and until mephenesin was available there was no drug that would produce it. During the stage of initial muscular rigidity, action currents are present in the resting muscle owing to central nervous system stimuli. However, later on these contracted (but not convulsing) muscles do not show action currents, thus representing the previously mentioned spastic states which take place without being influenced by stimuli arriving from the spinal cord, and which do not disappear until the nerve end-plates in the muscles either recover or degenerate and atrophy.

Thus, the continuous tonic rigidity of tetanus probably is caused by the effect of continuous minor stimuli to the muscles and their motor nerve end-plates, respectively. This is in contrast to the intermittent paroxysmal abnormal reflex muscular contractions or major convulsions arising from major motor stimuli that are attributable to a loss of inhibition of the interconnecting fibers of the intermediate neurons in the reflex arc, the so-called internuncial pool of nerve fibers within the spinal cord and medulla. There internuncial fibers permit a resultant and greatly enhanced, abnormal, gap-jumping, hyperirritability and motor response to sensory stimulation on their part.

Curare has been used to control this nerve-muscle end-plate involvement, but the author's clinical experience with curare has been disappointing, principally because there is no way known at present of telling when the paralyzing effect of the drug has passed: At one moment the patient's contractions are well-controlled, and the next he may die in severe convolution.

The characteristic opisthotonic convolution of non-sedated tetanus may result from any type of relatively insignificant sensory stimulus. It is exceedingly agonizing, and on x-ray examination, 20 per cent of all surviving patients are observed to have unsuspected fractures of the spine. If the respiratory muscles, including those of the hypopharynx and larynx, are involved in prolonged and severe convulsions, death commonly results from asphyxia. Retained secretions also cause pneumonia.

The sedative effect of drugs commonly used at present does not occur upon the cord until all functions of the cerebrum and the autonomic centers are first greatly diminished and the resulting deep narcosis has lowered blood pressure and diminished respiration. This unsatisfactory result is owing to aiming therapeutic bullets at the wrong target, and to using the wrong bullets. The paroxysmal reflex convulsions of tetanus which originate from sensory stimuli are a result of abnormal reflex response along the entire uninhibited abnormally excitable internuncial pathways to all the motor nerves. This abnormal response is owing to loss of inhibition and increased irritability of the intercommunicating or internuncial fibers in the cord and medulla, so that response of the motor component of the reflex is along all efferent pathways instead of just following its usual individual physiological channel. What is needed is a drug or drugs to break up this internuncial motor reflex linkage in the cord, from which a sensory stimulus results in a response of all the motor reflex arcs instead of just the physiologically normal individual one. The problem is to dampen and suppress the highly magnified nervous motor impulses originating in the cord as a result of this peculiar involvement of the internuncial fibers. Mephenesin accomplishes this.

However, when used in the dosages required for the control of tetanic convulsions, mephenesin causes trouble. It prolongs the phase of serum sickness over many days, and causes the concurrent appearance of maculopapular hemorrhagic rashes during that time. In addition, it increases the fragility of the erythrocytes, causing hemolysis, anemia, hemoglobinuria and, occasionally, death.

This led to a search for other drugs which would have the desired selective action upon the internuncial fibers instead of the cerebral centers, yet would not have toxic effects upon erythrocytes. One such was a preparation called Myocain. It had been used for this purpose by a group of Viennese physicians¹ in tetanus cases with most unusual results as follows: Mephenesin was used in 29 cases and the death rate was 4 per cent, while the death rate in a control group of 34 cases in which mephenesin was not used was 59 per cent. However, hemoglobinuria occurred in 11 of the patients who received mephenesin, and in 15 there was increased fragility of erythrocytes at the cessation of treatment. This led to using Myocain instead of mephenesin. In experiments with animals Myocain produced identical effects in its specific action upon the intercommunicating fibers of the cord, but without hemolytic side effects. Four patients with severe tetanus, all with an unfavorable prognosis, were given the drug. The paroxysms were controlled and all four recovered. Single doses given ranged from 1 gm. to 3 gm., given as a 2.5 per cent solution by continuous intravenous drip. The effect of a single dose was said to last three to 12 hours. The total dosage given in any 24 hours varied from 4 to 15 gm.

This report led the author to procure some Myocain from

its manufacturer, Dr. Holzinger of Vienna. Chemically, this substance is O-Methoxyphenylglycerol ether. A search in this country appeared to show that Resyl^{*} had the same molecular structure. Accordingly, Resyl rather than Myocain was substituted for mephenesin. The case herein reported upon is believed to be the first case of tetanus in which Resyl was used, and the result obtained indicates further investigation of this drug.

ADDENDUM

Since this report was written, six additional patients treated with Resyl have had excellent symptomatic relief. The only untoward effect noted was a tendency to cause simulation of paralytic ileus owing to the relaxing effect.

*This product was supplied for trial by the Ciba Company.

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EDITORIAL

The Proposed "Average Fee" Plan

THE SO-CALLED "AVERAGE FEE" PLAN brought before the meeting of the House of Delegates in December 1952 can be expected to receive wide attention at the coming meeting of that body. In the interval between meetings a systematic effort has been made by the California Medical Association and its component county societies to discuss the underlying reasoning which prompted a committee of 15 physicians working some 18 months to include this suggestion among the ten recommendations for changes in the structure of California Physicians' Service—"The Doctors' Own Plan."

Three of the ten recommendations have already been accepted. The first two place more responsibility on the California Medical Association for the operation of C.P.S. The House of Delegates for the C.M.A. is henceforward to be the same as for C.P.S. The C.M.A. Council similarly has now become a nominating committee for C.P.S. trustees.

The third recommendation already accepted is that the trustees of C.P.S. shall organize a medical care plan of *indemnity type*. A subsidiary recommendation to this one is the "average fee plan."

Any insurance plan to continue successfully must be on a sound actuarial basis. This may be accomplished by a per capita system or by a service or indemnity plan. The *per capita system*, widely used in England, may at first appear as the easiest means of attaining such a balance. This system is not unlike some "closed-panel" plans in our own country. The physician is paid so much per patient per year, sick or well. The evils of this kind of socialization and its tendency to make the less conscientious physicians give the "once over lightly" to so many patients per hour, are sufficiently understood by the profession to require no further consideration.

The *service plan* is the one under which the 11,000 physician members of C.P.S. now operate in caring

for patients with an annual personal income of less than \$3,600 or family income under \$4,200. The physician members bind themselves to accept a fixed fee schedule and agree to take a lesser percentage of this schedule if there is not enough in the "kitty" to pay the full unit value, as has often been true in the past.

Under the *indemnity type* coverage already in use by Blue Cross, and proposed for California Physicians' Service, the patient is paid by the insurance company. The doctor is then paid by the patient. This allows the patient to assume his usual role of paying the doctor, but the insurance company indemnifies the patient at least part way toward his medical and hospital expenses. *This is the arrangement which has been recommended and accepted.*

Now as to the "average fee for the average patient of the average physician" feature. An insurance company, when indemnifying a patient, must have some knowledge of the usual cost to it of a medical procedure or hospitalization. However, physicians vary widely in their ideas of the worth of their services. At present those who are loyal to C.P.S. remain members, and must not charge more than the fee schedule for those patients on the service plan. Those who do not feel the necessity for such loyalty resign from the plan and, therefore, automatically are on an indemnity basis.

The committee realized from the outset that fee schedules or compulsion of any kind is distasteful to all doctors. It is well-nigh impossible to arrange a schedule, for example, which will at the same time be fair to the recent graduate and the long-experienced practitioner of unusual attainments. County-wide "average fee" schedules are not entirely new, having already been adopted independently by some county societies on their own initiative. Industrial accident fees and those paid by Blue Cross and some

insurance companies have been with us for almost a generation.

By way of solving the insoluble, therefore, under the proposed plan any physician will be permitted to deviate from any state or county-wide fee schedule, so long as *the patient knows about it in advance*. Thus a physician may set up his own schedule, or have none at all for that matter. This basic independence permitting him to set his own fees has been considered a "must" by the independent American physician.

Most physicians have a fairly well fixed schedule of charges for procedures, which they alter upward or downward depending on a variety of circumstances peculiar to the community, on the practice of other physicians who do similar work and on such factors as the difficulty involved in treatment and the economic status of the patient.

Although preliminary discussion of fees to prevent later misunderstandings with patients has been a recommendation of the American Medical Association for a long time, the public and press have shown the "average fee" proposal an unexpected and rather extraordinary amount of interest.

It is to be hoped that the House of Delegates will give its most earnest consideration to the recommendations adopted already by so many of the county societies, and while not tying the hands of C.P.S. trustees by too much arbitrary or specific legislation, will nevertheless clearly set forth principles for their future guidance.

The Practice of Medicine

THE ART OF MEDICINE is caring for a patient, while the science of medicine deals with diagnosis and management of disease. Together they constitute the practice of medicine. For as long as medicine is practiced it will remain an art as well as a science.

The practice of medicine has become increasingly complicated in the last 50 years as the science of medicine has made available many instruments and diagnostic and therapeutic procedures that are costly to use and frequently demand the assistance of specially trained personnel. Increases in scientific knowledge in all aspects of medicine have come so rapidly and in such volume that it has been difficult for a single physician to keep abreast of those necessary for the care and treatment of his patients. With the pace of modern life there has been all too frequently a strain or even fracture of the patient-physician relationship which is the basis of the art of medicine.

These changes along with so many others characteristic of modern civilized life in the United States have greatly altered the practice of medicine. The trend has been, as it is in all complicated biological structures, toward a division of labor, toward specialization. In multicellular organisms, certain cells, tissues or organs assume certain specific functions for the good of the whole and immediately become dependent on other parts of the organism for essential functions which for them have become vestigial or non-existent. The unicellular organism, however, continues to perform all necessary functions for continuance of a life which, although it may be one of independence and freedom, is nonetheless one of rather limited horizon.

Largely because of the changes occurring in modern society and in medicine itself the practice of medicine has changed in ways that have led to the organization of physicians for the practice of medicine. These organizations may be in groups, in partnerships, in associations, in clinics, in open and closed panels, in and around hospitals and in parts of industrial and other concerns. Each method of practicing, be it that of the individual in general practice or of the salaried highly trained specialist in a large group, has advantages and disadvantages.

In light of the great interest in the subject of the practice of medicine, not only among the members of the medical profession but among the public as well, it seemed appropriate to present in CALIFORNIA MEDICINE a series of factual articles on various methods of practice in California. In the February issue an article on the Permanente Foundation was published. In this issue, features of the Ross-Loos Group in Los Angeles are described (page 477). Subsequently, with the continued cooperation of those responsible for them, it is planned to present factual material concerning the medical and hospital plans of the various railroads of California and of a closed panel group in San Francisco. Thereafter it is anticipated that there will be published data concerning other groups representative of clinics, partnerships, industrial and perhaps of individual practice of medicine.

The reader will find much interesting factual material in these presentations. In considering the various plans of practice, perhaps the final thought of the physician will be of the place of the patient-physician relationship in them. Is there free choice of physician? There is the keystone upon which the art of medicine depends. It is essential for the best practice of medicine no matter what the form of practice.

California MEDICAL ASSOCIATION

NOTICES & REPORTS

Cancer Detection

A Statement by the California Cancer Commission. An outline of methodology, implementation and potential value of cancer detection as a part of general health surveys

PRESENT RATES of cancer control are far short of what is theoretically achievable, particularly when the disease occurs in certain accessible sites. The case for cancer detection procedures is based on the premise that periodic physical surveys of asymptomatic persons would uncover concealed cancer at a curable stage in such numbers as to be a rewarding effort, commensurate with the time, effort and cost involved. Statistical evidence listed herein indicates that this objective can be reached, but only if there is an informed segment of the population which will persist in being screened year after year. It is obvious that only a minor fraction of the population will interest itself in such a regular program. Even if applied on a mass scale, the contribution to cancer control would represent only further fractional improvement in the total problem. In spite of these deficiencies, a significant effort in cancer case finding would decrease the lag between what is theoretically possible with present techniques of treatment and our present inadequate control of malignant neoplasms. A recent report¹ indicates that probably not more than 15 per cent of all cancer cases in California survive five years after the diagnosis is made.

Of those sites in which concealed or occult cancer may be found by a standard detection survey, the estimated gap between maximum cures with available knowledge and present cures is outlined below as modified from Steiner.²

Site	Per Cent of All U. S. Cancer Deaths, 1948	Per Cent Present Cures	Estimated Maximum Cures with Available Techniques, Per Cent
Breast	9.2	20	35
Uterus	8.2	35	75
Prostate	5.7	5	10
Skin	1.7	85	98
Mouth	1.5	15	40
Larynx	0.9	30	75

In addition to those sites accessible by standard physical survey, a common form of cancer can be detected by endoscopic examination—carcinomas of the anorectosigmoid segment of the colon. As approximately seven out of ten cancers of the colon and rectum are within reach of the finger and proctoscope, figures corresponding to those above may be estimated thus:

Large intestine 16.2% 20% 65%

The present average cure rate of cancer in these seven accessible sites is at present, then, about 31 per cent. If the maximum cures with available knowledge were secured through treatment at an asymptomatic stage, the cure rate should increase to about 57 per cent, or an almost two-fold increment in cures.

Some disparity between the theoretical and the achievable will always persist, for the difference represents a complex problem both in attitude and edu-

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cation of the public and the profession, as well as psychological and economic factors. In our present state of knowledge, the only effective means for improvement of end result is to bring the patient to effective treatment at an earlier anatomical stage of the disease, which can best be done when the process is still occult, or asymptomatic.

The public is being indoctrinated with the importance of detection procedures: it is the responsibility of the profession to provide periodic health surveys for those who seek such service. It should be emphasized that the objective should be the detection of incipient or occult disease in general, even though the theme of cancer detection may be the most effective lever in securing the interest of presumably well persons. In fact, many disease entities are more susceptible to discovery in an occult phase than is cancer. The most meticulous detection procedure offers only a 6-out-of-10 chance for locating asymptomatic cancer.

For this and other reasons born of experience, the Cancer Commission's philosophy is that detection procedures belong in the physician's office rather than in specially organized, impersonal "cancer detection centers." The operation of such centers primarily for the discovery of neoplastic diseases is illogical for other disease processes are uncovered with 10 to 20 times more frequency than are neoplasms. Cancer detection centers also fail generally in securing consecutive yearly examinations of any significant fraction of their examinees. Continuity of detection procedures can best be done in those who depend on their own physician for periodic surveys. Detection centers are unnecessarily costly, geographically discriminatory and frequently conducted by physicians with extremely limited interests.

In general, of course, the main burden of periodic health surveys will be borne by physicians in general practice, internists and general surgeons. The county medical society has an important function to perform in this respect, usually through its cancer committee. One of the major obstacles at present is that the public has no means of knowing which physicians are interested. A poll of the members of the county medical association should be obtained to set up a roster of physicians who are interested in cancer detection and periodic health surveys. Inasmuch as the American Cancer Society through its educational work is constantly receiving inquiries on this subject, it seems reasonable that the society and its information centers should be provided with a list of these interested physicians in each geographic area. This can only be done, of

TABLE 1.—*Points to Be Covered in a Cancer Detection Examination*

1. Skin
2. Lips and buccal cavity
3. Thyroid gland
4. Breast
5. Abdomen
6. Female pelvis
7. Male genitalia
8. Rectum and prostate
9. Lymph nodes which are accessible

course, with the approval of the county medical society. The function of the American Cancer Society, or any other voluntary agency, should be the demonstration of the need, the education of the public to its value, and in its function in bringing the prospective examinee and the doctor together. Economic considerations should be worked out by the county medical society with the panel of physicians so that no individual will be denied the benefits of a standard cancer detection examination.

The county medical society and its cancer committee must go considerably further than the mere listing of a panel of physicians who have expressed their willingness to do cancer detection examinations. The problem of what constitutes a satisfactory standard or minimum detection examination is something that should engage attention. Each of the physicians on the panel who are going to become cancer detectors should be furnished with information concerning minimum standards, and each physician should accept such standards as a minimum with such additions and elaborations as his own interests may dictate. In Table 1 are seen the nine points recommended for a minimum cancer detection examination. It is emphasized that these requirements are the absolute minimum which can be expected to produce a satisfactory yield of cancer of accessible sites, and represent actually less in the way of examination than that which is carried out by a physician who performs careful routine or annual physical examinations. It is not anticipated that these examiners will do less than they have been doing, but is rather hoped that those whose examinations do not include these points will see that they are added. Physicians to whom the problem of preventive medicine in the early detection of all types of chronic disease represents a challenge, will naturally broaden the examination in accordance with their time, facilities and particular interest.

From the standpoint of cancer detection alone, as one is dealing with a person who is presumably well, the formal taking of the history, a time-consuming procedure, is not productive enough to warrant its inclusion. Routine blood counts seem to offer no

value in cancer detection examinations, for only one examinee in many thousands will have unsuspected leukemia, for which we have only palliative measures at best. The presence of anemia of moderate degree is entirely non-specific and, in fact, the recording of hemoglobin values within normal limits in the presence of advanced cancer is commonplace.

Routine urinalysis is also of so little value as to be an unproductive phase of a cancer detection examination. Only catheterized specimens are of value, in which the microscopic finding of red blood cells would only indicate about 2 per cent of unsuspected cancers in the urinary tract, and again these inaccessible cancers are rarely curable.

Although the findings of Overholt indicate that carcinoma of the lung is more frequently surgically resectable when discovered in a silent phase by roentgenographic examination of the chest, this is of little value on a mass basis unless repeated every six months. Mass x-ray surveys of the chest have indicated that the yield of primary cancer of the lung will be only 10 in every hundred thousand persons examined. This is an incredibly small number when the expense involved is considered.

Proctoscopic examination, although not listed as part of the standard examination here, is strongly recommended since almost 70 per cent of all cancers of the colon, rectum and anus are within reach of combined examination by digital, anoscopy and proctoscopic procedures. The high incidence of polyps, both benign and malignant, in apparently

well persons is such that every doctor who becomes interested in cancer detection procedures should acquire experience in proctoscopic examination through its constant use.

As the statistical picture of cancer mortality is far from being a true representation of cancer as seen in practice, it is more pertinent here to consider the clinician's experience rather than the statistician's sample. In the male the sites of importance from the standpoint of hopeful prognosis are those of the skin, larynx, lip and oral cavity, and in the female the uterine cervix, skin and to a lesser extent the breast. The inaccessible sites are more common in the male. The lesser incidence for inaccessible sites in the female explains the failure of cancer mortality rates to yield in the male. For both sexes combined about 42 per cent of all diagnosed cancers are in accessible sites.

Realizing that almost 70 per cent of all cancers of the colon are within reach of digital and endoscopic examination, and assuming that examinees could have the benefit of visualization of the terminal rectosigmoid segment, about 55 per cent of diagnosed cancers would become detectable by inclusion of these procedures.

This provides the opportunity for some theoretical calculation as to what sort of impact a cancer detection examination, which includes proctoscopic examination and chemical testing of the stool for blood, would produce in a segment of the population which would submit regularly to such detection procedures. In Table 2 is shown the percentage of cancer mortality due to lesions primary in six accessible anatomical sites in the female. These combined sites account for 42.4 per cent of all female cancer deaths. Assuming the sort of cancer detection examination just described, and assuming effective treatment at an early stage because of discovery of these lesions while still in a silent phase, and accepting average reported five-year cure rates in such early lesions, the mortality should be reduced to 23 per cent. The theoretically achievable effect would be a reduction of almost 50 per cent in mortality from cancer arising in "accessible" sites in the female. Conversely stated, the increase in five-year survival from all cancer in the female should almost be doubled, from the present rate of 25 per cent to 45 per cent.

A similar theoretical predicted reduction in mortality for the male (Table 3) is not as encouraging. Only 30.6 per cent of all cancer deaths in the male are accounted for by lesions in these accessible sites, and the application of cancer detection methods would produce a reduction in mortality to 20.82 per cent or a reduction of one-third in cancer mortality from lesions originating in accessible sites. This

TABLE 2.—Showing: (a) Female Contribution to Mortality Rates from Cancer Originating in Six Accessible Sites, and (b) the Estimated Reduction Achievable by Treatment at an Early (Asymptomatic) Phase

Site of Cancer	Mortality Rate (Per Cent)	Estimated Mortality Rate with Detection (Per Cent)
Buccal cavity	1.4	0.39
Rectum, anus	4.3	2.58
Larynx	0.2	0.04
Uterine cervix	16.6	4.16
Breast	18.9	15.20
Skin	1.0	0.60
Total	42.4	22.97

TABLE 3.—Current and Calculated Mortality Rates for Males from Cancer in Five Accessible Sites, Compared to Table 2 for Females

Site of Cancer	Mortality Rate (Per Cent)	Estimated Mortality Rate with Detection (Per Cent)
Buccal cavity	5.0	2.10
Rectum, anus	8.2	4.92
Larynx	2.0	0.40
Prostate	13.7	12.40
Skin	1.7	1.00
Total	30.6	20.82

would nevertheless be a significant improvement in current poor five-year survival rates from cancer in the male, or from something under 20 per cent to a figure approaching 30 per cent.

CONCLUSIONS

1. Periodic cancer detection examinations limited to asymptomatic persons can be of distinct value as an adjunct phase of a cancer control program.

2. Its value is in the discovery of certain accessible cancers during their silent phase, thus bringing to definitive treatment a larger number of biologically favorable lesions while still actually limited to their anatomical sites of origin.

3. More cancers will be discovered by the widespread use of a minimum or standard type of examination than by the restricted use of a more elaborate examination.

4. Detection centers as currently operated contribute little toward education of the public or the profession, and render a minimum service because of the small number of examinees and their failure to continue periodic examination. A limited number of well organized detection centers may be of value in the future study of screening mechanisms for more efficient detection of silent cancers.

5. Cancer detection surveys are best done by interested physicians as part of office practice.

6. The county medical society should function to bring the public and the interested physician together by maintaining rosters of qualified, interested physicians preferably made available to local units of the American Cancer Society and its information centers.

7. By regular examination of a given segment of the population over a period of ten years, the cumulative yield of cancers discovered should approach 8 per cent, compared to about 0.2 per cent in most detection centers.

8. About 42 per cent of all cancers are accessible by a minimum physical examination.

9. With the addition of proctoscopic examination, about 55 per cent of cancers can become "accessible."

10. Uniform application of this more adequate survey would produce, by calculation, a decrease of 20 per cent in cancer mortality in women, and a 10 per cent reduction in men.

11. Cancer detection should be a phase of general, periodic, health surveys.

REFERENCES

1. Report to Cancer Commission, C.M.A., Breslow, L., Chief, Bureau of Chronic Diseases, Department of Health, State of California, 1952.

2. Steiner, P. E.: An evaluation of the cancer problem, *Cancer Research*, 12:455-464, July 1952.

The Ross-Loos Medical Group

A GROUP OF PHYSICIANS, associated in the form of a co-partnership, is engaged in the practice of medicine under the name of *Ross-Loos Medical Group*. It consists of 130 full-time staff members. All devote their full time to the practice of medicine and surgery, or to the administration of the affairs of the Ross-Loos Medical Group.

The purpose of Ross-Loos is to supply medical care to its patients (subscribers and dependents). In this sense it differs not at all from a private physician, whether he operate singly or with others. All patients pay for their services.

Ross-Loos does differ from almost all other medical groups in the manner of payments by its patients (its subscribers). Payment for services (both for groups and individuals) is based on a periodic payment plan. For this periodic payment (by groups and individuals) Ross-Loos agrees to take care of almost all medical and surgical services (there are certain specified exemptions) necessary for the patient.

All persons either in groups or as individuals desiring Ross-Loos medical service must make application for the service. No solicitation or advertising of any kind has ever been or will ever be engaged in by Ross-Loos. Ross-Loos conforms strictly to the ethics of the medical profession.

All subscribers are free to terminate the Ross-Loos service at any time. All patients of Ross-Loos have free choice in the selection of a physician or physicians from its large staff of more than 130 physicians. Consultants outside the staff are available at all times, and are frequently called in.

Ross-Loos is not a corporation, not a cooperative, not a non-profit organization. It is not a part of, nor is it subsidized by, any foundation, trust, religious, educational, political, or secular body, or government agency. It is not tax exempt and it neither seeks nor receives any support, grants, subsidies, or special favors from any unit of government—local, county, state or federal.

THE PHILOSOPHY OF ROSS-LOOS

The underlying philosophy of Ross-Loos was formulated by Drs. Donald E. Ross and H. Clifford Loos at the time the partnership was established, in 1929. That philosophy—or policy—has remained unchanged to this day.

This is one of a series of articles concerning methods of practice of medicine in California by physicians in groups, partnerships, organizations and individually. It was prepared at the request of the Editor, by the Ross-Loos Medical Group. Others will appear from time to time in CALIFORNIA MEDICINE.

The articles are for the information of members of the California Medical Association. Publication does not imply official approval or disapproval by the Association.

In the late 1920's there were few functioning plans anywhere in the United States which covered the contingency of illness for the average citizen. Organizations and institutions were already well developed and widely accepted which took care of many of the possible emergencies which might arise for the average person. However, there were, at that time, few plans by which the average man and his family could be protected against the financial hazards arising from illness and disease. The burden of doctor and hospital bills fell heavily upon people within the low and middle income groups.

Doctors and other health experts already knew and were proclaiming the need for preventive medicine.

The founders believed that effective preventive medicine could be achieved within the framework of existing medical practice and ethics, and without the need for governmental interference through some form of socialized medicine. They were also of the opinion that a structural set-up could be established that would sharply cut the yearly cost of medical care to the average family. It was only through the establishment of a group of doctors that this condition could be met.

The basic points in the Ross-Loos philosophy were and are:

1. To pool the combined skills and knowledge of a group of physicians, including specialists to care for their patients.
2. To render medical and hospital service to individuals through their voluntary affiliation with a health group or committee.
3. To establish a monthly fee for service, based upon estimated costs of rendering such a service.
4. The organization established to undertake this work should be owned, managed and controlled by doctors of medicine.
5. The same ethical rules which covered the individual practitioner should apply to each and every staff member of the group, and the group itself.
6. The organization should not engage in any advertising or in the solicitation of subscribers to its services.

The Ross-Loos Medical Group came into being April 1, 1929. Nearly a year earlier, several employees of the Los Angeles Department of Water and Power, inspired by former employees of the Southern Pacific Railroad which had a company health program, began an investigation among local physicians to see whether some type of group medical insurance plan could be developed. Among others

approached were Drs. Donald E. Ross and H. Clifford Loos, who had already been thinking along similar lines.

Many conferences took place between the employee group and these two physicians. Nearly a year was devoted to working out details before the Ross-Loos Medical Group was formally organized. Its first list of subscribers consisted of somewhat more than 400 employees of the Los Angeles Department of Water and Power.

The periodic fee paid by the members from the Department of Water and Power was \$1.50 per month. Medical service, conforming in every particular to the highest ethical standards, was made available to all subscribers. No fees were charged for medical services to their dependents at that time although the dependents paid for all drugs and hospitalization.

Subscribers to the Ross-Loos service encouraged other employees from the Department of Water and Power to join the health group.

Within a few months after its inception, an employee of the Los Angeles Fire Department (whose brother was a Ross-Loos subscriber from the Department of Water and Power) asked if Ross-Loos would accept a group of fire-fighters as subscribers. The two physicians then counselled with the employees' Health Committee of the Department of Water and Power, and obtained permission to enroll the fire-fighting group. Other groups followed and by the middle of 1932 the number of subscribers had increased ten-fold.

RULING ON CHARGES OF VIOLATING ETHICS

Group medicine, as practiced by Ross-Loos Medical Group, was largely a new venture in the early 1930's. Quite naturally most physicians did not understand it. Some of them feared its growth. Others charged Ross-Loos with violating the ethics of the medical profession by solicitation of membership through advertising and other means. In 1934 charges to this effect were brought against Drs. Ross and Loos by the members of the Los Angeles County Medical Association, and they were ordered expelled from the Association. The two partners appealed the decision and carried the case to the Judicial Council of the parent body, the American Medical Association. The highest body of the medical profession declared that the charges were not properly proven, that an adequate investigation had not been made and that proper procedure had not been followed. The Judicial Council then reversed the decision of the County Medical Association and ordered the physicians reinstated. This was done.

INDIVIDUAL SUBSCRIBERS ACCEPTED

Late in 1936 Ross-Loos Medical Group modified its structure to permit individual subscribers the use of its services. This change in policy grew out of the fact that large numbers of group subscribers lost their Ross-Loos membership when they changed jobs or retired. Many other Ross-Loos subscribers had friends or relatives who desired their services but were unable to function through any group as such. Increasing pressure from both of these sources grew with each passing year.

The decision to permit individual subscribers was taken only after long and careful consideration among the partners of the organization for it was feared that office and administrative overhead would increase the cost to individual subscribers very substantially. As a matter of fact, however, the rate for individual subscribers is usually no more than 50 cents per month above that of group subscribers.

At the close of 1952 Ross-Loos had 28,000 group subscribers and 9,000 individual subscribers. In addition, it is estimated that the average number of dependents per subscriber is 2.2. This means in actual fact, that there are between 125,000 to 130,000 patients who are regularly served by the Ross-Loos Medical Group.

NATURE OF ROSS-LOOS SERVICES

Subscribers to Ross-Loos services consist of: (1) those who subscribe through a group; and (2) those who subscribe individually.

There is no definite limit to the size of the group which makes application for medical services with Ross-Loos Medical Group, but anyone desiring membership within the group must sign an individual application for service. A contract or agreement is entered into between the official representatives of the group and the Ross-Loos medical organization.

The basis of accepting members in a subscribing group varies with the many factors of physical condition to be considered. Some of these are—whether the employer asks for a pre-employment physical examination; the stability of the employees; the male and female complement of the group; the age of the applying employees. All of these will influence whether the group can be taken without physical examination or whether any control will be exerted.

Once the members of the group have been accepted, Ross-Loos agrees that "The Medical Group shall furnish medical and surgical care and attention, including professional consultations, treatments, examinations, surgical procedures, and preventative care, including the following: Laboratory tests, x-ray examinations, physiotherapy treatments,

splints and dressings, consultations, eye examinations, ambulance service (for a distance not to exceed 15 riding miles traveled by a patient on any one trip), and hospitalization.

Hospitalization is declared to mean: A bed in a two-bed room, or a bed in a private room for semi-contagious diseases, in a first class hospital designated by the Medical Group, for a period not to exceed 90 days in any period of 12 consecutive months, including general nursing, x-ray examinations, laboratory tests, operating room, medical and surgical supplies, special diets, meals, anesthetics, electrocardiograms, physiotherapy treatments, hypodermic therapy, oxygen service, drugs, dressings, laboratory examinations, and all other adjuncts customarily given in ordinary hospital procedure.

Exemptions to the above are declared to consist of the following conditions or the results thereof: Dental care, insanity, chronic alcoholism, drug addiction, or attempted suicide. Ross-Loos does not furnish materials, procedures, or hospitalization if ordered by any doctor outside its organization. It will not supply special nursing care, sick room furniture, crutches, wheel chairs, orthopedic appliances, eye glasses, blood plasma for transfusions, hypodermic medication or drugs given outside of the hospital, radium, x-ray therapy, dental x-rays, hospitalization for cases of obstetrics, abortions, miscarriages, venereal diseases, mental diseases, contagious diseases, alcoholism, drug addiction or conditions arising therefrom or sanatorium or rest home treatment.

Subscribers are entitled to service at any hour of the day or night every day of the year, to all necessary home calls and office calls. Ross-Loos asks that the patient place himself within a radius of fifteen miles of any one of its designated offices to be entitled to service. In practice, this means that the subscriber can live almost anywhere in Los Angeles County.

Group subscribers are also entitled to special privileges at low fees for services rendered to their dependents. A dependent is defined as a spouse and children under 19 years of age. Each subscriber must list his dependents with the organization. The fee schedule for dependents is subject to change on 30 days' written notice to the subscribing group; but as a matter of fact such changes as have taken place have been due entirely to increased medical costs. No change has been made in these fees in spite of increasing costs since 1947.

Prior to World War II, dependents paid 75 cents for each office consultation or treatment. At present the following charges are made to dependents: \$1.25 for office calls, \$2.00 for daytime resident calls, and

\$2.50 for resident calls at night. Minor operations performed at the office (including surgery and recovery bed) cost not over \$20. Major operations cost \$25. Confinement cases, including prenatal and postnatal care, cost \$50.

The agreement between Ross-Loos and the subscribing group provides that the agreement may be cancelled and services terminated by either party by notice in writing given not less than 90 days prior to the date of cancellation. Ross-Loos may likewise cancel the subscription of any subscriber when any payment provided for is not paid when due. Any subscribers within a group may resign from Ross-Loos at any time by submission of a written notice to that effect from the subscribing group to Ross-Loos Medical Group.

Individual Subscribers: Any person between the ages of 21 and 50 is eligible for application (although a member of any group may transfer to individual membership regardless of age). A prospective member must first contact one of the offices of the Ross-Loos Medical Group either by mail, telephone, or in person to get an application form. This must be filled out and a physical examination undertaken. Individual subscribers pay \$3.00 for the examination plus a \$6.00 registration fee payable at the same time. In the event an applicant is not accepted as a subscriber, the registration fee is refunded. Individual subscribers pay a monthly fee of \$6.00, payable on the first day of each month for the preceding calendar month.

A subscriber may terminate his subscription upon 30 days' written notice to the Ross-Loos Medical Group. The Medical Group in turn may terminate its services to the subscriber upon 30 days' notice in writing. However, should a subscriber be under treatment for an illness or injury on the effective date of termination, Ross-Loos agrees to continue its services for a further period of 60 days.

All individual and group subscribers receive identification cards for themselves and their dependents. These are presented by the patient when requesting service. Medical services given to individual subscribers are the same as those given to group subscribers.

THE STRUCTURE OF ROSS-LOOS

At its inception in 1929, and continuing through until approximately April 1, 1936, the organization was a co-partnership of Dr. H. Clifford Loos and Dr. Donald E. Ross. Early in 1936 that co-partnership was widened. Sixteen members of the staff were taken into the partnership. During the next decade

or so, the personnel of the partnership underwent several changes due primarily to death and disability. At the present time, there are 12 partners.

General control of Ross-Loos is in the hands of the partnership. The partners meet once a week to consider business affairs and the general operation of the organization. In making decisions all partners have only one vote each.

Due to the size of its operations, the partnership established a number of sub-committees (usually of three doctors each). These sub-committees include: Finance, Hospitalization, Personnel, Purchasing, Housing, Maintenance and Scientific.

Dr. H. Clifford Loos acts as administrator and with the help of the partners handles all problems of administration and control. Dr. Donald E. Ross is the chief surgeon and, assisted by the partners and staff, devotes his time to the medical, surgical, and scientific interests of the organization.

For many years now, the work of the physician members of the group has been divided into the following departments: General practice, internal medicine (including cardiology, gastroenterology, endocrinology, etc.), surgery, obstetrics-gynecology, ophthalmology, otolaryngology, pediatrics, dermatology, urology, allergy, neuropsychiatry, x-ray, proctology, orthopedics, and physical medicine.

STAFF MEETINGS

Regular meetings are held monthly and all staff members are expected to attend. At these meetings papers are read and reports given on matters concerning the entire medical staff. Outside speakers of note are often invited. Sectional and departmental meetings are likewise held at regular intervals to deal with specific problems relating to work and study in each field. In addition, bulletins and inter-office memoranda are used to inform staff members of anything of importance not discussed at regular meetings.

CHARTS AND MEDICAL CASE HISTORIES

The medical record of every patient is kept on a chart. Each subscriber is given a chart number. This number is also used by his dependents. The subscriber's charts are kept at the Ross-Loos office to which the patient usually goes for medical service. A master file of all subscribers and dependents is maintained at the central office. Each physician makes his own entries on the medical case history chart at the time he examines the patient. Notations are also entered by the laboratory or x-ray departments at the time their services are used.

DEPARTMENTALIZATION OF SERVICES

Home calls, whether day or night, are obtainable by merely calling any office of the group. Special members of the office staff route and schedule these calls from the home-call doctors to speed the service and avoid unnecessary travel by the doctors. The home call office always checks on the patient the following day to find out whether additional services are needed.

Nearly ninety per cent of all Ross-Loos patients are examined or treated at one of its offices in the course of a year.

Minor operations requiring hospitalization for less than one day are performed in the surgery department of the main medical building, where there are 20 recovery beds to take care of patients.

Ross-Loos does not maintain its own hospital, nor does it intend to build one. Nearly all its patients are sent to Queen of Angels Hospital.

Ross-Loos maintains two departments in connection with hospitalization. One of these is devoted entirely to arranging for ambulance service, getting the bed at the hospital, and informing the doctor or surgeon of the time, place and location of his patient at the hospital.

The second is the Medical Record Department which records and tabulates all pertinent information and statistics in connection with hospitalization, major and minor surgery, and diagnosis. Both before and after operation, this vital statistical material gives every doctor a breakdown of necessary information regarding every hospitalization case he or any other member of the staff has attended to. The standard medical index pattern is used in recording these cases. Such records have been maintained since the inception of Ross-Loos. At present, two full time librarians are employed for this work. All material in the Ross-Loos Medical Record Department is available to all members of its staff for research and study or in the preparation of scientific books, articles or monographs.

All records and accounts at the outlying offices are identical in form and they are handled in the same manner as are those in the central office. They constitute, in fact, an integral part of the whole organization. Duplicate general records are kept on each patient and his dependents, one set of which is on file at the main office.

All bookkeeping, accounting and purchasing are handled from the main office in close cooperation with the sub-offices.

Doctors and nurses in the sub-offices maintain regular, daily telephonic contact with the medical specialists and departments at the central office.

THE ROSS-LOOS CLIENTELE

Ross-Loos subscribers represent a good cross-section of the population of Los Angeles County. Almost all nationalities are included.

Occupationally, they include university and college professors, high school and elementary school teachers, policemen, firemen, city and county civil service employees, Department of Water and Power employees, librarians, dairy workers, bakers, engineering employees, aircraft employees, retail market employees, postal employees, rubber workers, oil workers, motion picture employees, radio network employees, insurance company employees, astronomers, bus drivers, consumer groups, real estate groups, brokerage house employees, and many others.

Individual subscribers represent every walk of life from unskilled laborers to bankers.

The majority of group subscribers are civil service employees or teachers. Most other groups, too, are made up of skilled or professional workers in occupations or industries where there is relative job security and low turnover. Such stability and security make for greater security and stability of the medical group itself.

THE SUBSCRIBERS' HEALTH COMMITTEE

The key to successful group medical practice and the maintenance of effective liaison between Ross-Loos and its patients lies in the Subscribers' Health Committees.

The Health Committee is the direct, active, responsible representative of the subscribers. Every group which wishes to obtain for its members (and their dependents) the medical services of Ross-Loos, no matter how large or small, must first select or elect a Health Committee to act as official spokesman for the group.

It is the Health Committee which works out details of the written agreement entered into between the subscriber group and Ross-Loos. It is the Health Committee which assumes responsibility for collecting dues from its members and turning these fees over to Ross-Loos. This procedure enables the Health Committee to keep a close and accurate tab on its members.

The Health Committee performs another invaluable function in that it serves as a clearing house for questions, complaints and suggestions from its own members. Subscribers make known their wants and complaints more freely to such a committee than to the medical or administrative staff of Ross-Loos. The Health Committee can quickly and easily transmit these suggestions, questions or complaints to the proper authorities of Ross-Loos for action. This

procedure is a valuable time saver for all concerned and is also a means for speed and efficient action. Tensions and misunderstandings between patients and the doctors can be cleared up quickly with a minimum of friction.

By means of the Health Committee Ross-Loos is enabled to discover weaknesses within its own staff (medical, technical, or administrative) in their dealings with group subscribers. The administrative heads of Ross-Loos then have an effective means of finding out if its services are reaching the people, as well as the degree of satisfaction or dissatisfaction with all or any part of it. In other words, by means of dealing with group subscribers through their Health Committees, Ross-Loos is able to give its members better service; a quick and direct approach for solving their problems. At the same time it provides Ross-Loos with a means to check and control its own services.

Health Committees for the various groups affiliated with Ross-Loos hold regular meetings (usually once a month) at which they discuss their problems with representatives of Ross-Loos. It is their job, as the direct representative of the subscribers, to make sure that these subscribers know about and obtain all services to which they are entitled.

Health Committee members perform their jobs on a volunteer basis, although some of the larger groups maintain a full time or part time employee to handle records and accounts. In such instances, members of the group usually assess themselves a small quarterly fee to cover this overhead. Ross-Loos will not do business with any group which charges its members a fee over and above the absolute minimum necessary to cover such office expense.

When interested individuals approach Ross-Loos about group membership, they are not automatically accepted as members. Quite to the contrary, they are urged first to check and study the many insurance and medical plans now available to them, including Ross-Loos, to determine which one most nearly meets the needs of their group. If, after such study, they are convinced that Ross-Loos will best fulfill their needs, the administrative representatives stand ready to discuss details with them and work out the basis for a group agreement. It is explained that members of their group who wish to join must individually make out an application form.

It has been proved by actual practice over a period of nearly a quarter century that the Health Committee is one of the cornerstones to successful group periodic payment medicine, because it offers an efficient and democratic method of communication between the subscriber and the medical group itself.

THE MEDICAL STAFF

No matter how efficient and effective all other parts of the medical group, its heart and center is the medical staff. The selection of new members for the medical staff is the responsibility of the Personnel Committee of the partnership. In the selection of such men the committee demands the following qualifications:

Physicians must have graduated from an approved medical school.

They must have served at least a year's internship in an accredited hospital.

They must have served a one-year residence in an accredited hospital.

Finally (though this last point is not always strictly adhered to), they must have been out of medical school for not more than seven years. In specialties where more training or experience is desired, this does not apply.

In short, Ross-Loos wants young physicians who have had the benefit of relatively recent training and internship, tempered by a few years of active medical practice.

There are at present 118 doctors on a salary basis. Each is given his own private office and examination rooms; each is provided with the necessary nurses and office help; and each works a regular forty-hour week. In addition, all doctors are on an emergency schedule to cover nights, holidays and week-ends.

Doctors are encouraged to practice medicine in the manner they were taught; but above this, they are given the added advantage of close association and consultation with a host of other doctors and specialists, as well as technical and laboratory facilities such as no individual doctor ordinarily possesses.

Some staff doctors have contracts with Ross-Loos. These contracts are worked out to meet mutual interests of the individual doctor and Ross-Loos. In addition to the salary (which is comparable with and oftentimes exceeds that paid by other institutions) every staff doctor receives a two-week vacation with pay each year during the first five years of employment; three weeks' vacation with pay each year for the next five years; and four weeks' annual vacation with pay after ten years of employment. The group likewise maintains a life and total disability insurance policy for him, for which the group pays more than half the premium. The doctor automatically becomes a subscriber (without charge) to Ross-Loos and is entitled to all its advantages. After three years' service with Ross-Loos, he becomes a joint participant in the profits of the organization.

All doctors joining the staff are assigned work

either as general practitioners doing home call work from the central office (either night or day); as general practitioners in one of the twelve branch offices; or as a specialist functioning in the main building. So far as possible, doctors are placed in areas where they wish to live. Such preferences are filled on the basis of seniority. Although some doctors who function in the outlying offices are specialists, general medicine is practiced at these offices. Most patients requiring the attention of specialists are referred to the downtown offices.

THE TECHNICAL AND ADMINISTRATIVE STAFF

Nurses, pharmacists, x-ray, medical and laboratory technicians receive not less than the prevailing wage scale. They work forty hours a week. They automatically are entitled to free subscription to Ross-Loos medical services; group insurance, for which the organization pays more than half; and two weeks' vacation with pay each year. Similar working condition and benefits are granted all other employees.

In the selection of all non-medical personnel, technical competence and experience are a basic requirement. Pleasing and cooperative personalities are likewise important in dealing with large numbers of patients who require service each day of the year.

PERSONNEL AND PATIENT RELATIONS

One of the major problems to which Ross-Loos has devoted much time and attention has been how to attain and to maintain the direct, personal intimate contact between physician and patient. This relationship, as every physician knows, plays a very important part in establishing the proper rapport between physician and patient.

Ross-Loos has attempted to meet this problem in many ways. First and foremost has been its insistence that each subscriber have a free choice, insofar as possible, in selecting from among the large staff the physician whom he likes best. The physician, in turn, comes to know these patients intimately. To all intents and purposes they are *his* patients. In the second place, all staff members and other personnel are constantly reminded that Ross-Loos patients must be treated with both courtesy and efficiency.

At the time the Ross-Loos Medical Group was first established in 1929, and for the first ten years of its existence, its major problems consisted of the following:

1. How to interest physicians in associating with such a radical and untried experiment.

2. How to overcome the general hostility of the medical profession and the public indifference to group medicine.

3. To determine how complete should be the medical coverage given groups subscribing for Ross-Loos services.

4. How to determine in advance an adequate monthly fee to the subscribers which would be low enough to be attractive to them, yet high enough to enable the group to attract good doctors.

5. To determine the extent of the area which could be covered in terms of service and home calls.

6. To arrange for speedy and adequate hospitalization.

Within a year's time it was realized that the original monthly fee was inadequate to give proper medical care to the subscribers and their families. Medical and hospital expenses mounted rapidly. For example, in 1930 Ross-Loos paid \$2.75 a day for hospitalization of its patients. Now the rate exceeds \$25 a day. At intervals as they have occurred these increased costs were explained to the Health Committees. New proposals were made which were acceptable to the committees, which, in turn, helped

work out new fees commensurate with the services being given.

Additional problems now faced include:

1. The threat of governmental interference in the practice of medicine.

2. Richly subsidized defense plants and governmental agencies which can and do set the standard of price for physicians, nurses, technicians, receptionists, secretaries and other help.

3. The aging population of the country at large and the higher average age rate of the subscriber groups.

Solution to the last of these problems has been partially met by use of a sliding scale of dues.

To attract and hold efficient personnel, various incentive programs have been devised as well as reducing hours of work, increasing pay, and giving all employees numerous other benefits.

How to meet the continued encroachment of government in the field of medicine is one which obviously cannot be solved by the Ross-Loos Medical Group nor even by the medical profession as a whole. It must be solved by an enlightened citizenry.

In Memoriam

ANDREWS, HENRY J. Died in Los Angeles, February 28, 1953, aged 74. Graduate of Northwestern University Medical School, Chicago, Ill., 1907. Licensed in California in 1909. Doctor Andrews was a retired member of the Los Angeles County Medical Association and the California Medical Association, and an associate member of the American Medical Association.

BRENNEMAN, RICHARD E. Died in Sawtelle, February 15, 1953, aged 79. Graduate of Harvard Medical School, Boston, Mass., 1900. Licensed in California in 1939. Doctor Brenneman was a retired member of the Los Angeles County Medical Association and the California Medical Association, and an associate member of the American Medical Association.

COLVER, BENTON N. Died in Los Angeles, March 14, 1953, aged 82, of coronary artery disease. Graduate of the American Medical Missionary College, Battle Creek, Mich., and Chicago, Ill., 1904. Licensed in California in 1925. Doctor Colver was a member of the Los Angeles County Medical Association, the California Medical Association, and the American Medical Association.

HARDIN, CLAUD E. Died in New York City, March 2, 1953, aged 59. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1930. Licensed in California in 1930. Doctor Hardin was a member of the Stanislaus County Medical Society, the California Medical Association, and the American Medical Association.

HUGHES, HERBERT A. Died in San Diego, March 20, 1953, aged 47. Graduate of the University of Oregon Medical School, Portland, 1939. Licensed in California in 1940. Doctor Hughes was a member of the San Diego County Medical Society, the California Medical Association, and the American Medical Association.

MEYENBERG, WERNER D. Died in Salinas, February 10, 1953, aged 56, of coronary occlusion. Graduate of the University of California Medical School, Berkeley-San Francisco, 1926. Licensed in California in 1926. Doctor Meyenberg was a member of the Monterey County Medical Society, the California Medical Association, and the American Medical Association.

PENDERGRASS, JAMES E. Died in Clovis, December 16, 1952, aged 56, of coronary thrombosis. Graduate of Vanderbilt University School of Medicine, Nashville, Tenn., 1921. Licensed in California in 1921. Doctor Pendergrass was a retired member of the Fresno County Medical Society and the California Medical Association, and an associate member of the American Medical Association.

TEEL, AMBROSE W. Died in Redlands, March 24, 1953, aged 81. Graduate of the College of Physicians and Surgeons, Keokuk, Iowa, 1895. Licensed in California in 1900. Doctor Teel was a retired member of the Los Angeles County Medical Association and the California Medical Association, and an associate member of the American Medical Association.

NEWS & NOTES

NATIONAL • STATE • COUNTY

ALAMEDA

Dr. Clement A. Smith of Boston will be visiting lecturer for the second annual **Clifford Sweet Lectureship** at Children's Hospital of the East Bay in Oakland, May 20 to 22. Beginning at 10 a.m., Wednesday, May 20, the program will continue with both morning and afternoon meetings through Thursday and Friday at the hospital. The Sweet Lecture will be given Friday evening, following dinner, at the Salem Room, Hotel Claremont, Berkeley. Dr. Smith's subject will be "The Newborn Infant."

All sessions will be open to physicians who wish to attend. Reservations for the Friday night dinner and lecture may be made through Children's Hospital of the East Bay, 5105 Dover Street, Oakland 9, California.

LOS ANGELES

Dr. Clinton H. Thienes, director of Huntington Memorial Hospital, Pasadena, was elected a vice-president of the Walter Reed Society at the annual meeting of the organization held last month in Chicago. The society is made up of persons who have served as voluntary subjects for experimental research.

* * *

The Los Angeles Dermatological Society in conjunction with the Metropolitan Dermatological Society of Los Angeles is having a luncheon for visiting dermatologists on the third day of California Medical Association's Annual Session, May 24 to 28, in Los Angeles. The luncheon will be at the Hotel Clark, Hill Street and Fifth, Tuesday, May 26, from noon to 2 o'clock.

* * *

The California Chapter of the American College of Chest Physicians will meet at the Hotel Biltmore, Los Angeles, Wednesday, May 27.

The program follows:

MORNING Business Session

Culture Media for Growing Mycobacteria—Drake Will, M.D.; Wm. Dunn, M.D., and Emil Bogen, M.D., Los Angeles.

Serum Protein Alterations in Pulmonary Tuberculosis—I. Alfred Breckler, M.D.; Alfred Goldman, M.D.; Eric Stern, M.D., and Mr. Robert Robison, Los Angeles.

Roentgenologic Alterations of the Lung Associated with INH Therapy in Pulmonary Tuberculosis—David Salkin, M.D., and Joseph A. Schwartz, M.D., Los Angeles.

New Trends in Rehabilitation of Tuberculosis Patients—John H. Aldes, M.D., F.A.C.S., and Lorrain M. Huntley, B.S., O.T.R.

Virus Infections of the Lung—A. F. Rasmussen, Jr., M.D., Los Angeles.

AFTERNOON

Selection of Patients for Mitral Commissurotomy—David C. Levinson, M.D.; Alfred Goldman, M.D.; Morley Kert,

M.D.; Jerome N. Sugarman, M.D.; Jack A. Scheinkopf, M.D., and Maurice H. Rosenfeld, M.D., Los Angeles.

The Use of a 20 to 30 Degree Reduction in Body Temperature in Cardiac Surgery—J. Francis Dammann, Jr., M.D.; Marvin Darsie, M.D., and William H. Muller, Jr., M.D., Los Angeles.

Cardiac Resuscitation—Sanford E. Leeds, M.D., San Francisco.

Diagnostic Problems and Therapy of Pulmonary Embolism—John J. Sampson, M.D., San Francisco.

Studies on the Resistance of Pulmonary Tissue to Ischemia—Harry A. Davis, M.D., Los Angeles.

A Correlation of the Spatial Vectorcardiogram with Right Ventricular Hypertrophy—Stephen R. Elek, M.D.; Bertram J. Allenstein, M.D., and George C. Griffith, M.D., Los Angeles.

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Following is the program for the **California Heart Association's** annual scientific meeting to be held the afternoon of Wednesday, May 27, in the Southern California Edison Auditorium, 601 West Fifth Street, Los Angeles:

2:00—Presidential Address—Lewis T. Bullock, M.D., Los Angeles

2:10—Acute Pericarditis—B. E. Pollock, Colonel, MC, San Francisco.

2:30—Changing Patterns of Sodium Metabolism in Essential Hypertension—Daniel M. Green, M.D., Los Angeles.

3:00—Use of Pressor Agents in Myocardial Shock—John J. Sampson, M.D., San Francisco.

3:20—The Pathogenesis of Hypercholesterolemia: Introduction of a New Concept—Meyer Friedman, M.D., Sanford C. Byers, Ph.D., and Ray H. Rosenman, M.D., San Francisco.

3:50—Intermission.

4:00—Discrepancy Between the Electrocardiogram and the Clinical Condition of the Patient—Myron Prinzmetal, M.D., Los Angeles.

4:25—Metabolism of the Human Heart in Vivo—Richard J. Bing, M.D., Guest Speaker, Professor of Experimental Medicine, University of Alabama, Birmingham.

SAN FRANCISCO

Writing on "Chemotherapy of the Eye," William Howard Spencer, third-year student in the University of California School of Medicine, won first prize in the 1952 Schering Award contest. The annual competition, which last year was open to undergraduate students in 83 medical schools in the United States and Canada, was begun in 1944 by the pharmaceutical firm to encourage the preparation of reports by medical students as a step in training for contributions to the medical literature.

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Dr. O. W. Jones, Jr., associate clinical professor of neurological surgery at the University of California School of Medicine, was elected president of the Society of Neurological Surgeons at the society's annual meeting held recently in New Orleans.

* * *

The 24th annual postgraduate symposium on heart disease will be held at the St. Francis Hotel, October 28 and 29, 1953. The San Francisco Heart Association, which has presented this annual postgraduate series for 23 years, has this year invited five Northern California heart associations

to participate in bringing to San Francisco a large contingent of distinguished guest speakers for the occasion. Sharing the planning with the San Francisco Heart Association will be the heart associations of Alameda County, Contra Costa County, Monterey County, San Mateo County and Santa Clara County.

Four guest speakers have already accepted the invitation to participate. They are Doctors Herman Blumgart of Boston, Howard Burchell of Rochester, Minnesota, Robert L. King of Seattle, and Paul Wood, Dean of the Institute of Cardiology, London.

* * *

Dr. Howard C. Naffziger was elected president of the American Surgical Association at its meeting last month in Los Angeles.

GENERAL

The annual session of the Gerontological Society will be held August 25 to 27 in the Mark Hopkins Hotel, San Francisco. Announcement of the meeting said that the program will include papers by outstanding authorities on the biology of aging, the medical problems and the psychological, social, and religious aspects of growing old.

* * *

The fifth annual convention of the International Academy of Proctology will be held at the Plaza Hotel, New York City, May 29 to 31, immediately preceding the annual meeting of the American Medical Association. A surgical clinic and seminar will be held May 28 at Jersey City Medical Center under the direction of Dr. Earl J. Halligan. An extensive motion picture seminar of proctologic surgery (including office techniques) will be held May 31. Because general practitioners, as well as gastroenterologists and proctologists, encounter proctologic problems in daily practice, much of the program has been planned to answer their questions. All physicians are invited to attend.

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The annual meeting of the Western Orthopedic Association will be held at Sun Valley, Idaho, October 5 through October 8, 1953. Further information may be obtained from the office of the Secretary, 1301 Spring Street, Seattle 4, Washington.

* * *

The tenth annual meeting of the American Geriatrics Society will be held at the Hotel Commodore, New York City, May 28 to 30. The first two days will be devoted to scientific papers and discussions. The annual dinner will be held Friday evening, May 29. On Saturday afternoon the society is invited to see the work being done at the William I. Sirovich Day Center, 203 Second Avenue, New York City.

* * *

A special committee of the California Medical Association which worked out standardized methods of measurement of joints for use in evaluation of compensation claims has been holding meetings with the various county medical societies, in cooperation with the California Indus-

trial Accident Commission, to present the methods and explain their use.

The committee has expressed a willingness to appear before groups particularly interested in compensation evaluation.

Further information may be obtained from Dr. Packard Thurber, chairman, 111 West Seventh Street, Los Angeles.

POSTGRADUATE EDUCATION NOTICES

MEDICAL EXTENSION UNIVERSITY OF CALIFORNIA

Postgraduate Courses for 1953

Pediatric Conference, June 22 through 26. Fee to be announced. Medical Center.

Conference on General Surgery, June 15 through 19. Fee \$75.00. Medical Center.

Obstetrical and Gynecological Conference, September 2, 3, 4. Place and fee to be announced.

Ophthalmology (for specialists), September 14 through 19. Fee \$75.00. Medical Center.

Medicine for General Practitioners, September through November. East Oakland Hospital. Fee \$50.00.

Evening Lectures in Medicine, September through November. Fee \$50.00. Mills Memorial Hospital, San Mateo (probably).

Contact: All inquiries to be addressed to Stacy R. Mettier, M.D., Professor of Medicine, Head of Postgraduate Instruction, Medical Extension, University of California Medical Center, San Francisco 22.

STANFORD UNIVERSITY SCHOOL OF MEDICINE

Cardiology—Date: June 15-19. Fee: \$75.00.

General Medicine—Date: June 15-19. Fee: \$75.00.

Surgery of Trauma—Date: June 22-26. Fee: \$75.00.

General Surgery—Date: June 22-26. Fee: \$75.00.

Programs and further information may be obtained from the Office of the Dean, Stanford University School of Medicine, 2398 Sacramento Street, San Francisco 15, California.

UNIVERSITY OF CALIFORNIA AT LOS ANGELES MEDICAL EXTENSION in cooperation with SCHOOL OF MEDICINE

Laboratory Technicians' Symposium—

Date: June 20 and 21 (all day)—UCLA Campus.
Fee: \$15.00.

Contact: Dr. Thomas H. Sternberg, Head of Postgraduate Instruction, Medical Extension, University of California, Los Angeles 24.



THE PHYSICIAN'S Bookshelf

THE TREATMENT OF DIABETES MELLITUS—9th Edition. Elliott P. Joslin, A.M., M.D., Sc.D., Medical Director, George F. Baker Clinic, New England Deaconess Hospital, Clinical Professor Emeritus, Medicine, Harvard Medical School; Howard F. Root, M.D., Associate in Medicine, Harvard Medical School; Priscilla White, M.D., Sc.D., Instructor in Pediatrics, Tufts College Medical School; and Alexander Marble, A.M., M.D., Clinical Associate in Medicine, Harvard Medical School. Lea and Febiger, Philadelphia, 1952. 771 pages, \$12.00.

This ninth edition of Joslin's classic book on diabetes still occupies the number one position among the books on diabetes.

It seems as though everything regarding diabetes is mentioned, and there are innumerable references to all phases of diabetes. Actually the only omission this reviewer could find was that the distinction between the glucose tolerance tests of liver disease and of diabetes was not too clearly defined.

The book is unduly long and some parts seem rather laboriously written, and it is also true that one can't sit right down with it and find quickly how to treat a new diabetic. Nevertheless, it is hard to imagine anyone treating many diabetics without having this book handy as a frequent reference.

It is truly a "must" as a handy reference book for any internist or general practitioner.

* * *

OPERATING TECHNIQUE—Fourth edition. St. Mary's Hospital, Rochester, Minn. W. B. Saunders Company, Philadelphia, 1952. 345 pages, \$6.50.

This excellently gotten up little book fulfills its purpose in every way. Its authors state that in the operating rooms at St. Mary's Hospital uniformity and simplicity of procedure are stressed with allowances for the preferences of the surgeon and requirements of the patient. Excellence, uniformity, simplicity and clarity are the chief virtues of this volume.

The specialist in gynecological surgery may object to having his operations included in the procedures in general surgery, the younger surgeon trained in operations on the large bowel may wonder what a "Kraske" operation is, the surgeon particularly interested in the gastrointestinal field may affect surprise at the employment of three layers of suture in gastrointestinal anastomosis. Others may check a flaw here and there according to their own beliefs, but the present reviewer is going to leave the book just as it is and congratulate the staff of St. Mary's Hospital on their work in the operating room and in the compilation of this book. In operative surgery it is vital to hold fast to that which has been proved sound, at the same time accepting what is good as well as new. This book does both these things admirably.

Attention is called particularly to the excellent illustrations which with the help of a sympathetic surgeon should aid nurses in understanding the procedures in which they

play so vital a part. Chapter eight on the "Surgical Team" with its outline of the duties of the surgical assistants and the operating room nurses, is excellent.

To make the book perfect, any operating room supervisor or surgeon may make the few deletions and marginal additions she or he fancies—for which a short pencil sharpened only once will suffice.

* * *

VIRAL AND RICKETTSIAL INFECTIONS IN MAN—2nd Edition. Edited by Thomas M. Rivers, M.D., Director of the Hospital, Rockefeller Institute for Medical Research. J. B. Lippincott Company, Philadelphia, 1952. 719 pages with 90 illustrations, including seven plates in color, \$7.50.

The first edition of this book was a landmark in medical teaching since it was the first correlated comprehensive description of viruses, rickettsia, and the diseases caused by them which was suitable for students and practitioners of medicine. It is midway in scope between the more recent, more brief work, "Virus and Rickettsial Diseases," by Bedford and his associates, and the monumental review, "Virus Diseases of Man," by van Rooyen and Rhodes. Every student and physician should be familiar with these three books. The volume under review is most suitable for their own shelves since it contains adequate but not excessively detailed information about all phases of virus disease—clinical, microbiological, immunological, and epidemiological. In addition, it is very reasonably priced because of a subsidy from the National Foundation for Infantile Paralysis.

The Second Edition is 132 pages longer than the first and contains four new chapters: Hemagglutination of Viruses, Interference Between Animal Viruses, Diagnosis of Viral and Rickettsial Diseases, and the Coxsackie Group. Spot checking of many chapters reveals a substantial revision throughout the book and every important advance in knowledge with which the reviewer was familiar and for which he sought was included in the text. The chapter on poliomyelitis has been completely rewritten and includes some handsome color photographs of the pathology of the disease.

Paper, printing, and binding are of excellent quality, and the numerous illustrations are beautifully done. No typographical or errors of fact were discovered. The book may be highly recommended. Those who already own the first edition will not find sufficient new information in this volume to require replacement unless they are particularly interested in the field of virus and rickettsial disease, or responsible for teaching about it.

* * *

LOW FAT DIET COOK BOOK. Dorothy Myers Hildreth and Eugene A. Hildreth, M.D. Medical Research Press, 100 Park Avenue, New York, 1952. 148 pages, including 12 pages for notes, \$2.95.

This book is devoted entirely to suggested menus and recipes on a low fat diet. The recipes look good and any patient inflicted with a low fat diet could obtain useful information from this book. There is no point in a doctor reading it unless he just wants to look at recipes.